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SPACE BIOLOGY AND AEROSPACE MEDICINE

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LINEAR DISCRIMINANT FUNCTION USED TO ASSESS COSMONAUT REACTION TO LBNP

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (mansucript received 21 Jan 81) pp 4-6

[Article by A. D. Voskresenskiy, V. A. Degtyarev, V. G. Doroshev, N. I. Vikhrov, Zh. V. Barsukova and N. A. Lapshina: "Evaluation of Reaction to LBNP in Cosmonauts With the Use of Linear Discriminant Function"]

[Text] More than 10 hemodynamic parameters are recorded when the LBNP [lower body negative pressure] test is performed. For this reason, efforts to formalize the procedure of summarizing data in order to express the ultimate evaluation of the reaction to LBNP by a single digital value are completely justified. Formulas have already been proposed for orthostatic tests, in order to obtain overall digital evaluations, which are based on either discriminant analysis of data [1], or use of empirical scales, which permit expression of changes in various physiological parameters by a single scoring system [2]. The linear discriminant functions proposed to summarize the results of an orthostatic test can, theoretically be also used to rate reactions to LBNP. It has been shown [1, 3] that the link between scoring of reactions to orthostatic tests and LBNP on the first days after long-term bed rest is expressed by coefficients of correlation in the range of 0.63-0.75. However, to analyze the dynamics of cosmonauts' reactions to LBNP during flights, it is desirable to have formulas of overall ratings that would reflect both the specifics of the test and group distinctions of the tested individuals. Proceeding from these considerations, we have undertaken an attempt here to find effective linear discriminant functions (LDF) to assess the reactions to LBNP from the results of examining cosmonauts who have performed long-term orbital flights.

Methods

The detailed scheme for discriminant analysis and examples of application thereof to physiological studies were submitted previously [1]. A so-called instructive sample of observations is needed to find the LDF that would permit evaluation of the reaction to LBNP according to the set of hemodynamic parameters. It must consist of at least two groups (or classes) of observations [cases], which are known to differ in reactions to LBNP but are formed independently of the results of hemodynamic measurements. In this study, the fact that the cosmonauts had performed a long-term orbital flight serves as the criterion of formation of the "instructive sample." The first class consisted of 25 observations made when performing the LBNP tests before flights and the second, 25 observations made within the first few days after returning to earth. Each case was characterized by a set of nine hemodynamic parameters measured at the time of maximum increment of heart rate (HR)

under the influence of LBNP--35 mm Hg. This set was chosen on the basis of preliminary statistical analysis of preflight and postflight data. The selected parameters included the following: HR (per min), the period of ejection (EP, in ms), increments of HR (ΔHR/min), minimum (ΔAP_m) and pulse arterial pressure (ΔAP_p, mm Hg), rate of propagation of pulse wave in elastic vessels (ΔR_e, cm/s), expulsion period (ΔEP, ms), stroke volume (ΔSV, mℓ) and minute volume (ΔMV, in ℓ/min).

As a result of analysis of the "instructive sample," we found the LDF: $Y - 0.181 \cdot HR - 0.07\ \Delta HR - 0.054\ \Delta AP_m - 0.172\ \Delta AP_p + 0.007\ \Delta R_e + 0.013\ EP + 0.04\ \Delta EP - 0.115\ \Delta SV - 0.58\ \Delta MV$.

We then calculated the values of Y for each case in the "instructive sample" using a program of discriminant analysis run on a computer, and we found the boundary value (Y), which makes it possible to separate the preflight and postflight classes of cases in a statistically optimum manner.

The validity of the found rule for separation of classes was confirmed by the results of analysis of a control sample of cases. Then the found LDF was used to assess 36 reactions to LBNP tests conducted during space flights.

The increment (Δ) was found as the algebraic difference between values of the parameter during the test and at rest before the test.

Results and Discussion

The discriminant function serves to classify the cases [findings]. In the presence of the required set of parameters, each new case can be described by the evaluation of y. This value is compared to the values of y in the classes of the "instructive sample." On the basis of comparison, we can determine to which class a given case corresponds or is closer. The distribution of values of y in the "instructive sample" is illustrated in Figure 1. As we see, the values of y increase from class I to class II. The mean value of y is 16.43 for preflight findings and 20.6 for postflight observations. The differences between classes for the set of parameters is statistically reliable with a high level of significance ($F_{experim} < F_{0.001}$). Thus, the LDF we found can be used to classify reactions to LBNP.

Theoretically, the optimum boundary for separation of classes is $y_b = 18.51$. Indeed, only 5 cases in the class of preflight observations have a value of more than 18.51 for y and only two in the postflight class have a value of less than 18.51. Consequently, when using $y_b = 18.51$ as the criterion of classification, we can state with relatively little risk of error that cases of $y<18.51$ correspond to the class of preflight reactions and those of $y>18.51$ are referable to the class of postflight reactions to LBNP. Classification rules of this sort are used in diagnostics and mass scale surveyes, when a choice must be made between the conclusions, "healthy" and "sick." In physiological studies, there is usually no need to necessarily accept one of two possible answers. Since the ranges of the first and second classes partially overlap one another, it is expedient to define the range of uncertain answers [solutions, decisions], when determination of the class involves a substantial risk of error. Analysis of the distribution of y in the classes of the "instructive sample" (see Figure 1) enables us to offer $y = 17.5$ (bottom) and and $y = 19.5$ (top) as the range of this area. In the preflight cases, only one rating exceeded 19.5 and in the postflight class, only one was below 17.5. Thus, the evaluations exceeding the range of uncertain solutions can be referred to one of the classes with very little risk of error.

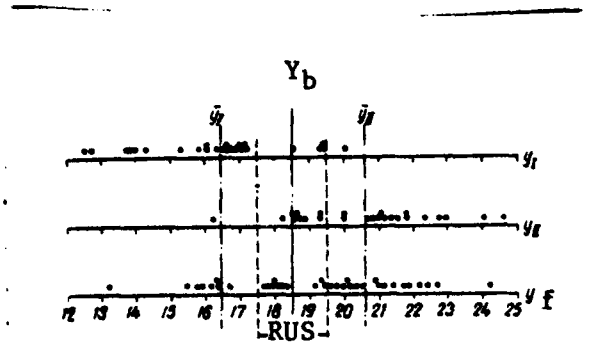

Figure 1.
Distribution of LDF values in classes of instructive sample and in group of flight cases:

Y_I and Y_{II}) classes of pre- and postflight cases, respectively
Y_f) flight data
Y_b) theoretical boundary between classes
Y_I and Y_{II}) mean value in classes I and II
RUS) region of vague solutions

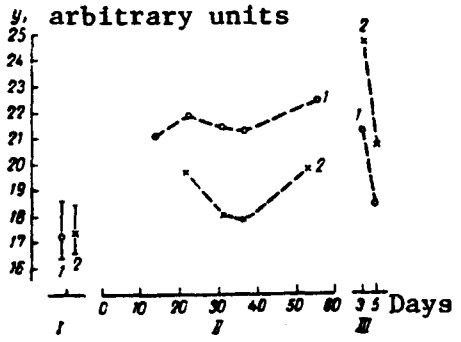

Figure 2.
Dynamics of evaluations of reactions to LBNP in the CDR (1) and FLE (2) of the second crew aboard Salyut-4
I) preflight
II) in flight
III) postflight

The scores obtained by means of LDF for reactions to LBNP in flight are also illustrated in Figure 1. As can be seen, these ratings vary over virtually the entire range of the "instructive sample." The minimal value (y = 13.26) obviously corresponded to preflight reactions and the maximal (y = 24.4) to postflight ones. However, only 9 reactions could be referred to class I with low probability of error and 17 to class II. The remaining 10 evaluations were referable to the region of uncertain solutions. Thus, the distribution of y during flight was generally closer to the postflight distribution. It is a known fact that the reaction to LBNP increases significantly after long-term flights. Consequently, the shift in value of y in the direction of the postflight class may signify intensification of inflight reactions to LBNP. Analysis of the dynamics of evaluation of reactions to LBNP as a function of time spent in weightlessness was difficult to perform because of the difference in duration of missions. The available data did not enable us to derive a conclusion that there was a tendency toward accentuation or attenuation of reaction in the course of the flight. The data illustrated in Figure 2 show that there were no unidirectional changes in flight or major individual differences in evaluations. The curves reflect the dynamics of reactions to LBNP of the second crew aboard Salyut-4. In the preflight period, the mean scores for the commander (CDR) and flight engineer (FLE) were quite close. During the flight, the values of the reactions of the CDR rose drastically and were above the top of the preflight range. The reaction to the first postflight test remained accentuated, whereas the one to the second test was almost normal. In two cases, the FLE presented a moderately accentuated inflight reaction to LBNP, whereas in two others it did not exceed the preflight range. However, the postflight reactions were drastically intensified, and the one to the second test was even more marked than the maximum inflight reaction.

Each of the parameters contained in the set used offers some information about the differences between the classes of prefight and postflight findings. LDF combines this information in an optimum fashion in the estimates of y, which is achieved by consideration of the "weight" (delimiting capacity) of different parameters and correlation between them. The scores obtained by means of LDF were characterized by similarity of a given case to one or the other class. They were always more accurate and reliable than the values of different parameters or linear combinations thereof with intuitively selected weight coefficients. Nevertheless, even for the set of nine hemodynamic parameters, the preflight and postflight classes were not entirely demarcated. This is not an unexpected finding. The mean values for these classes are reliably different. However, the difference in mean values reflects nothing other than the difference between the standards for normal and accentuated reactions to LBNP. It is not surprising that the reaction to LBNP is sometimes accentuated in a healthy individual during the stressful period of pre-lift-off preparations. On the other hand, we could expect that some cosmonauts would retain a normal reaction to LBNP even after a flight, by virtue of their individual distinctions. There may also be considerable variation of the reaction to LBNP from test to test in the postflight period, with a wave-like process of recovery of cardiovascular functions [4-6]. It should be noted that comparable results were obtained when a distinction was made between reactions to functional tests before and after long-term hypokinesia in ground-based studies [1]. The use of LDF increases the objectivity of scoring reactions to LBNP and makes it possible to express the dynamics of these ratings in a form convenient for analysis. Of course, interpretation of the dynamics of ratings obtained by means of LDF requires consideration of individual distinctions of cosmonauts and specific conditions, under which the tests are performed.

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COMPARISON OF DIRECT AND INDIRECT METHODS OF MEASURING CARDIAC OUTPUT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 24 Nov 80) pp 7-9

[Article by V. G. Doroshev, N. N. Popov, V. P. Katuntsev, N. A. Lapshina, O. B. Kulikov, G. K. Chizhov, V. A. Galichiy, K. S. Yurova and R. I. Finogenova]

[English abstract from source] In anesthetized dogs, cardiac output was measured directly (by the method of Fick and by electromagnetic flowmetry) and indirectly (by the method of Bremser-Ranke and by rheography). The measurements were carried out before and after drug tests. The absolute values of cardiac output at rest differed depending on the method used. After the drug test all the methods revealed distinctly changes in cardiac output. A good correlation between flowmetric and rheographic methods was demonstrated. In view of this, they can be recommended to be used in rapidly changing hemodynamic situations. The method of Bremser-Ranke proved more suitable for the processes developing within 30-40 seconds.

[Text] Indirect methods of measuring cardiac output are gaining increasing popularity in clinical practice. Their advantage is that they can be repeated many times and they are not traumatic. Rheograms, tachooscillograms, kinetocardiograms and sphygmograms of the femoral and radial arteries were recorded aboard manned orbital stations on Polynome-2M equipment and the Levkoy-3T rheograph, which made it possible to determine cardiac output by the method of Bremser-Ranke as modified by N. N. Savitskiy [1] and by the Kubicek method [2]. However, some objections have been made to the use of indirect methods, in view of the fact that they are not accurate enough and cannot be used dynamically, i.e., when hemodynamics undergo rapid changes.

The method of Bremser-Ranke, as modified by N. N. Savitskiy, was compared to the method of Grollman [3] and dye dilution method [4]. The authors obtained comparable results and recommended it for clinical use, particularly for children.

The same statements were made in favor of the Bremser-Ranke method, as compared to the method of Starr [5, 6]. At the same time, discussion is still continuing as to the suitability of the Bremser-Ranke method for dynamic studies, in particular when there are hemodynamic changes related to redistribution of blood. There are works, in which a comparison was made of the rheographic method to the methods of Fick, dye dilution, radioisotope method and use of flowmeters [7-9]. Comparisons

have been made of the results with the use of the Bremser-Ranke method to the rheographic method [10, 11]. The authors preferred the rheographic method as being more flexible when there is redistribution of blood.

Our objective here was to compare tachooscillographic and rheographic methods to direct ones (Fick and electromagnetic flowmetry). This comparison was made before and after giving pharmacological agents.

Methods

Studies were conducted on 11 mongrel dogs weighing 16-25 kg under morphine-nembutal anesthesia (0.5 mℓ 1% morphine per kg weight, 20 mg/kg nembutal intraperitoneally) with artificial ventilation of the lungs.

Cardiac output was measured in the base state, after giving drugs and after dissection of the chest, using two indirect and two direct methods simultaneously. The indirect methods were tetrapolar rheography and mechanography; the direct methods were the Fick method and measurements with electromagnetic flowmeters.

The following equation was used to calculate minute volume by the Fick method (in mℓ/min):

$$Q = \frac{\dot{V}_{O_2} \times 100}{Ca_{O_2} - C\bar{v}_{O_2}}$$

where $\dot{V}_{O_2}$ is oxygen uptake (mℓ/min), Ca_{O_2} and $C\bar{v}_{O_2}$ are oxygen content of arterial and mixed venous blood, respectively.

$\dot{V}_{O_2}$ was measured for 1-2 min on a Beckman MMC metabolograph. To determine Ca_{O_2} and $C\bar{v}_{O_2}$ simultaneously with recording of $\dot{V}_{O_2}$, blood samples were taken during the same period through catheters introduced into the aorta and pulmonary artery, and they were analyzed with micro-Astrup equipment of the Radiometer Company and Van Slyke equipment. Nihon Kohden probing flowmeters were introduced into the aortic arch. After measurements were taken in the base period and after intake of drugs, thoracotomy was performed in the fifth intercostal space on the left. We dissected the pericardium and isolated the ascending part of the aortic arch, over which we placed the sensory of the type MF-26 Nihon Kohden electromagnetic flowmeter (clip) to check the measurement of cardiac output.

An RPG-202 rheoplethysmograph was used to record rheographic signals. The electrodes are secured over the perimeter at the base of the neck and lower margin of the sternum to exposed [shaved?] parts of the skin to which contact paste had first been applied. The generator electrodes were 2 cm distal to the measuring ones.

A tachooscillographic cuff connected to a piezoceramic sensor was applied to the upper part of the front leg. The cuff was compressed by means of an automatic pressure device for 30-40 s.

The parameters were recorded simultaneously on an RM-150 polygraph (Nihon Kohden) and Mingograph-34.

A mixture consisting of 1 mℓ cordiamine, 10 mℓ 40% glucose and 10 mℓ saline was used as the pharmacological load to alter cardiac output. We administered 3-10 mℓ of the mixture, depending on the animals' weight and effects on them.

Results and Discussion

We compared the results of simultaneous measurement of cardiac output by the direct and indirect methods.

In addition to statistical processing, we compared pairs of readings of cardiac output for each sample and analyzed correlations between absolute and relative values of this parameter.

It was established that there were no statistically significant differences between readings obtained at rest by the Fick method, tachooscillographic (TM) and rheographic (RM) methods, or between readings obtained by the Fick and RM methods after the pharmacological test.

All of the above methods showed an increase in cardiac output after administration of pharmacological agents. After the pharmacological test, cardiac output increased by 46% according to the flowmeter test, 37% by the Fick method, 42% by the RM and 26% by the TM.

We tested the hypothesis that the difference between pairs of values for cardiac output obtained by the above methods equal zero. It was demonstrated that there were no statistically significant differences between the Fick method and TM or between the Fick method and RM at rest. After the pharmacological test there were also no statistically significant differences between the Fick method and TM.

Analysis of correlation between absolute values of cardiac output revealed that the coefficient of correlation between the Fick method and RM was $\rho = 0.55$ with $P<0.01$. The coefficient of correlation was about the same ($\rho = 0.51$), when we compared the relative (percentile) values of cardiac output obtained by flowmetry and the Fick method, flowmetry and TM ($\rho = 0.55$), Fick method and RM ($\rho = 0.58$). The coefficient of correlation was higher when we compared cardiac output measured by the flowmetric method and RM ($\rho = 0.73$, with $P<0.001$).

Thus, the results of these studies enabled us to conclude that there could be differences in absolute cardiac output when measured only once, and that they depend on the method selected to measure it.

Cardiac output measured by the Fick method, RM and TM was virtually the same in absolute value.

The increased cardiac output after the pharmacological test indicates that, regardless of the measurement method used, there is distinct demonstration of the orientation of changes during dynamic observation.

The rather reliable correlation between the flowmeter method and RM is attributable to the fact that these methods permit calculation of cardiac output for virtually every cardiac contraction and they are more suitable in the case of rapidly changing hemodynamic situations.

The Fick method and TM can yield only average values for cardiac output within a particular segment of time. It is inexpedient to use them in rapidly changing hemodynamic situations for methodological reasons; however, these methods are quite suitable for observing slow processes, when cardiac output remains virtually unchanged.

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UDC: 612.141-06:612.275

EFFECT OF NEGATIVE PRESSURE AND OCCLUSION CUFFS ON INTRAVASCULAR PRESSURE IN LEGS OF HEALTHY MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 23 Dec 80) pp 9-12

[Article by V. Ye. Katkov, V. V. Chestukhin, E. M. Nikolayenko, S. V. Gvozdev and V. V. Rumyantsev]

[English abstract from source] The effect of local negative pressure on the leg (with a bladder sealed above the knee) and occlusion cuffs (located as close as possible to Poupart's ligament) on the leg intravascular pressure was investigated in recumbency. In two experimental runs 8 healthy volunteers participated. Each of the two exposures was used at two levels: local negative pressure at -50 and -100 mm Hg and occlusion cuffs at +40 and +60 mm Hg with exposure time averaging 5-7 min. Catheters were inserted into the femoral artery and vein, and arteries and veins of the back of the foot. The arterial pressure remained unchanged during both exposures: local negative pressure and occlusion cuffs. Upon exposure to local negative pressure the venous pressure in the back of the foot (with respect to the atmospheric pressure) did not change and in the femoral vein decreased. Upon exposure to occlusion cuffs the venous pressure in the back of the foot increased noticeably and in the femoral vein decreased slightly. It is concluded that none of the exposures can reproduce the major gravitational effect on leg vessels, i.e. characteristic changes in gradients of the intravascular (transmural) pressure.

[Text] The following are the most important reactions occurring in the vessels of the legs of a healthy subject under the influence of gravity (orthostatic test): typical change in gradients of intravascular (transmural) pressure; increased volume of capacitive vessels and blood in them; slower blood flow and greater arteriovenous difference for O_2 [1-3]. It is known that some means of prevention of the adverse effects of weightlessness, in particular, negative pressure or occlusion cuffs (OC) applied to this region, can elicit the same changes in blood volume and blood flow; however, the question of how they affect intravascular pressure has not been explored. And this is understandable since there are, for example, many methods for recording blood volume (plethysmographic, radioisotope, ultrasound, rheographic and others), whereas only one (catheterization) is used to measure pressure in vessels of this region. At the same time, since gravity has a direct effect on only one circulatory parameter--the hydrostatic component of blood

pressure, changes in the latter should be considered the chief ones in the genesis of gravity-caused hemodynamic changes.

Our objective here was to study the effect of negative (subatmospheric) pressure and OC on intravascular pressure in the leg of a healthy subject.

Methods

This study was conducted on 9 healthy male subjects (average age 34 years, height 177 cm, weight 78 kg, body area 193 cm^2). Catheters (Odman-Ledine) were introduced in the femoral artery and vein, cannulas (Medicut) into the artery and vein of the dorsum of the foot under x-ray monitoring.

Two series of tests were conducted with each subject in horizontal position 20 min after catheterization. In the first series, we tested the effect of local negative pressure (LNP) in the region of the lower leg and foot (closing bag [bladder] right above the knee) constituting -50 and -100 mm Hg for 10-min exposure to each level (Figure 1). Electric manometers were outside the LNP bag, i.e., pressure in vessels was measured in relation to atmospheric pressure. We tested the effect of OC 20-30 min after termination of LNP, placing the cuffs as close as possible to the inguinal ligament and using pressure of +40 and +60 mm Hg for 10 min each (see Figure 1).

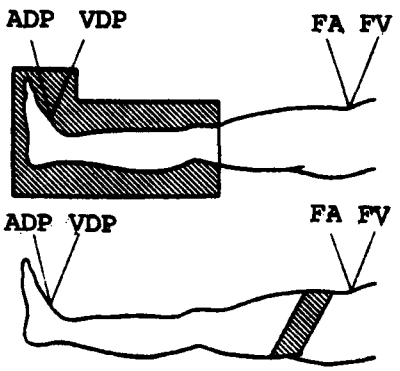

Figure 1.
Diagrammatic illustration of use of LNP (top) and OC. Here and in Figure 2:
VDP, ADP) vein and artery of dorsum pedis, respectively
FV, FA) femoral vein and artery

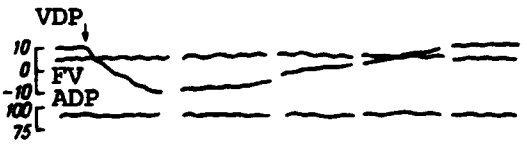

Figure 2.
Pressure (mm Hg) in vein of dorsum pedis, femoral vein and artery of back of foot during decompression. Arrow shows start of LNP. Explanation given in the text.

Vascular pressure was measured with Statham P23 Db electric manometers situated on the level of the right atrium. We recorded oxygenation parameters (American Optical Company).

The results were submitted to mathematical processing by the method of Student-Fisher, and Student's t criterion was used for statistical analysis.

Results and Discussion

Local negative pressure: The start of decompression was associated with immediate and usually marked drop of pressure in the vein of the back of the foot, whereas the other parameters did not change appreciably (Figure 2). In the next 2-4 min, this parameter reverted to the base level, where it remained throughout the test period.

After both modes of LNP, mean pressure in femoral vein presented a tendency toward decline, while pressure in other vessels was close to the base level (Table 1). With LNP of -50 and -100 mm Hg, oxygenation of hemoglobin in blood from femoral vein diminished, whereas in arterial blood it did not change, which led to increase in

Table 1.
Pressure (mm Hg) in different vessels of the lower limb under the influence of LNP

Parameter	Base level	LNP	
		−50 mm Hg	−100 mm Hg
FV	5,9±0,6	4,9±0.5	4.7±0,6
VDP			
(n=5)	12,0±2,0	11,0±2,5	10,6±2,3
FA			
s	129,6±3,6	127,8±3,5	129,0±3,1
d	79,4±2,6	78,5±2,9	78,0±3,0
m	96,3±2,0	94,8±1,8	95,1±1,7
ADP			
s	145,4±3,3	147,4±2,6	146,1±2,8
d	74,4±2,7	75,1±2,5	76,8±4,3
m	92,9±1,8	92,4±1,7	92,0±2,2

Key--for this and Tables 2 and 3:
FV) femoral vein
VDP) vein of dorsum pedis
FA) femoral artery
ADP) artery of dorsum pedis
s) systolic pressure
d) diastolic pressure
m) mean pressure

Table 2.
Pressure (mm Hg) in different vessels of the lower limb under the influence of OC

Parameter	Base level	OC	
		+40 mm Hg	+60 mm Hg
FV	5,2±0,7	4,8±0,7	4,3±0,7
VDP			
(n=4)	11,3±1,6	17,0±2,2	26,8±4,3*
FA			
s	128,3±2,5	127,0±2,1	124,5±3,3
d	80,8±3,2	81,0±3,9	81,2±3,7
m	94,7±1,4	97,0±2,0	93,3±1,7
ADP			
s	144,3±3,0	145,8±2,7	145,8±2,0
d	75,0±2,3	76,0±3,9	76,8±3,7
m	90,5±1,2	92,2±1,9	90,5±1,6

arteriovenous O_2 difference in the leg by 11 and 16%, respectively.

In this study, the leg vessels can be divided into two groups: vessels directly exposed to LNP (foot) and vessels upon which LNP had an indirect effect (thigh).

It is generally considered that negative pressure to tissues raises transmural pressure in vessels (difference between intravascular and extravascular pressure), simulating the effect of gravity on them. The fact that negative pressure affects vessels is unquestionable; however, there are still some serious questions that are unanswered. They include the following: how deeply does negative pressure penetrate into tissues, how does this change general tissular pressure and one of its most important components, pressure of intercellular fluid; what are the sequelae of regular exposure (LBNP training) in such a complex system as the intercellular space, which is the "safety valve" of the cardiovascular system.

We know of only one attempt made to measure pressure of intercellular fluid under these conditions [4]. Coles [5], who used needles, demonstrated that negative pressure penetrates into tissues to a depth of at least 2.5 cm, and 10% of it is lost. It must be noted that this method of measuring pressure of intercellular fluid was criticized by Guyton [6], who proved that it can only be used when pressure rises and that it is unsuitable to measure drops of this parameter.

The extremely marked, though transient, change in pressure in superficial veins (in relation to atmospheric pressure) indicates that they are not indifferent to this factor. Evidently, at the very start of decompression, their pressure rises proportionately to the change in pressure in the LNP bag, which leads to drastic increase in vein capacity. This is associated with increased filling of these vessels and slower blood flow in the lower extremity, as indicated by the increase in arteriovenous O_2 difference in this region.

The results we have obtained from this study do not enable us to define the transmural pressure in deep vessels, particularly the artery of the dorsum pedis. At the same time, it should be noted that if negative pressure does not penetrate deep into tissues one could hardly discuss its significant conditioning effect on one of the main local mechanisms that protect microcirculation against gravity factors, which, as we know, is in the region of the fine arteries, arterioles and precapillary sphincters [7].

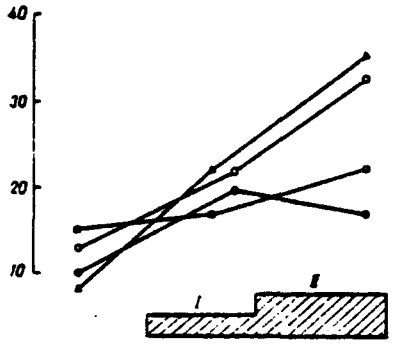

Figure 3.
Individual changes in pressure (mm Hg) in vein of dorsum pedis with the two pressures (I, II) in occlusion cuffs (striped area)

Table 3.
Effect of orthostatic test, 75° (Δ, ortho) and OC in mode of +60 mm Hg (Δ, OC) on pressure gradients (mm Hg) in leg vessels

Pressure gradients	Factor	
	Δ. ortho	Δ. OC
FA--ADP	—77	0
VDP--FV	63	19
FA--FV	12	—1
ADP--VDP	27	—19

There was virtually no change in intravascular arterial pressure in the femoral region, upon which LNP had a mediated effect, whereas venous pressure had a tendency toward decline. This is quite different from the changes observed with the orthostatic test, when vascular pressure in this r[illegible] rises appreciably, and to a greate[illegible]ent in the artery than the vein, [illegible] a result of which the arteriovenous gradient of intravascular pressure increases by 12 mm Hg (15%) [1].

Occlusion cuffs: The use of OC led to an appreciable elevation of pressur[illegible] in the vein of the dorsum pedis; pressure in the femoral vein presented a tendency toward decline, while arterial pressure in leg vessels did not change (Table 2). It must be noted that the pressure reactions of veins of the dorsum pedis to this factor presented some individual differences (Figure 3). With the use of OC in the modes of +40 and +60 mm Hg, oxygenation of femoral vein hemoglobin diminished and arteriovenous O_2 difference increased by 10 and 13%, respectively.

The use of OC in the indicated modes apparently elicited occlusion chiefly of superficial veins. This led to accumulation of blood in them and partial "elimination" from circulation, with subsequent run-off of a certain volume of blood over the deep veins. Of course, under such conditions, the state of the latter is an important factor, which determines individual changes in vessels of the limb as a whole.

The most vivid changes were observed in pressure in the vein of the dorsum pedis, which rose appreciably. It is known that virtually the same changes are observed in this region during the orthostatic test, so that the impression may be formed that these factors have identical effects. However, in our opinion, one should use changes in pressure within vessels of the region as a whole, rather than at some particular point, for a more correct comparison. Table 3, in which data obtained from our previous study are used [1], makes such a comparison. On its basis,

it can be concluded that the effect of the orthostatic test on pressure gradients in vessels of the lower extremity is not the same as the effect of OC.

With an individual in erect position, there is an increase in capacity of vessels (chiefly veins) of the leg, increase in volume of blood in them and slowing of blood flow under the influence of a gravity factor (hydrostatic component of blood pressure), as a result of which there is a decrease in venous influx of blood to the heart and central blood volume. Similar changes in central circulation are elicited by other factors: negative pressure and OC over the legs, breathing at excess pressure, bloodletting, etc. The use of negative pressure and OC is also associated with an increase in volume of veins and slowing of blood flow in vessels of the lower extremity. However, apparently none of these factors is capable of reproducing the main effect of gravity on vessels of this region--change in gradients of hydrostatic (transmural) intravascular pressure.

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EFFECT OF LOWER BODY NEGATIVE PRESSURE (CHIBIS GARMENT) AND LOCAL NEGATIVE PRESSURE ON CENTRAL CIRCULATION IN HEALTHY MAN

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[Article by V. Ye. Katkov, V. V. Chestukhin, E. M. Nikoalyenko, S. V. Gvozdev, V. V. Rumyantsev and Ye. V. Kolpakov]

[English abstract from source] Catheters were chronically implanted into pulmonary and radial arteries of 8 healthy volunteers to examine the effect of lower body negative pressure (LBNP in the Chibis suit) and local negative pressure on the leg on central circulation, oxidative metabolism and acid-base equilibrium in the blood. In 1-hour head-down tests (at -20°) the effect of two regimens of LBNP (at -30 and -60 mm Hg) was studied, each exposure averaging 15-20 min. Both LBNP and local negative pressure induced changes in central circulation that were similar qualitatively and dissimilar quantitatively. The use of regimen I of both exposures caused more marked changes than that of regimen II.

[Text] Lower body negative pressure (LBNP) has gained wide use for the prevention of the adverse effects of weightlessness. Local negative pressure (LNP) can be used for the same purpose, applied to different parts of the body, mainly the lower extremities; however, its effect on circulation has not been sufficiently investigated. There are two main goals for the use of these preventive measures: reduce central blood volume and raise transmural pressure in vessels of the lower limbs, i.e., create the hemodynamic situation that is similar to the one that occurs during an orthostatic test.

Our objective here was to examine the effects of different modes of LBNP and LNP on central circulation and compare these effects to changes that are observed during the orthostatic test.

Methods

We conducted this study on eight healthy male subjects (average age 34 years, height 177 cm, weight 78 kg, body area 193 cm^2). A two-way Swanvanz catheter with thermistor (Edwards Lab.) was implanted for several days in the pulmonary artery through the subclavian vein (puncture) and a special cannula (Medicut) was inserted in the radial artery with monitoring of x-rays and pressure curve.

Three series of studies were conducted for 3 days: control (series 1), with LBNP (series 2) and LNP (series 3). In all of the series, after recording the parameters in horizontal position we performed the orthostatic test (70° tilt, 15 min) then the turntable was rapidly moved to antiorthostatic position, -20° [head down] for 1 h. In the first series, no other factors were used during this period. In the other series, we tested the effects on central circulation of two modes of LBNP and LNP--mode I (-30 and -60 mm Hg, respectively) and mode II (-50 and -100 mm Hg)--after 20 min of head down position (background). Each of the modes was used for 20 min ("stable" state), and the parameters were recorded for the last 5 min of this period. During change of LBNP and LNP modes at the rate of 10 mm Hg per 10-20 s ("transient" periods), we recorded continuously central venous pressure, as well as pressure in the pulmonary artery.

The Chibis garment (LBNP) was sealed at the level of the iliac crests, and the LNP bag was sealed just above the knee.

Pressure was measured with Statham P23 Db electric manometers, which remained on the level of the right atrium throughout the test period. Minute volume of the heart has measured by the thermodilution method using the Edwards Lab. computer and simultaneous recording of the dilution curve. Right ventricular function and blood oxygen level were determined with the usual formulas.

We recorded the parameters of acid-base equilibrium of blood (micro-Astrup), hemoglobin content and oxygenation (American Optical Co.).

We used Student's t criterion for statistical analysis.

Results and Discussion

In the control study, the change from orthostatic to head down position was associated with changes in virtually all circulatory and mixed venous blood oxygenation parameters, whereas acid-base balance did not undergo appreciable change (Table 1). Throughout the head-down position, all of the recorded parameters remained at the same level and did not differ from values recorded in the 15th-20th min of exposure to this factor.

In the next series, the changes in recorded parameters were about the same as in the control for the first 15-20 min after changing from orthostatic to antiorthostatic position (background).

Use of LBNP or LNP was associated with immediate drop of central venous pressure and pressure in the pulmonary artery, the degree of which was not the same (Figure 1). It should be noted that, in the presence of drastic changes in these parameters, the heart rate either failed to change or increased in the case of relatively marked LBNP, i.e., at the time when significant changes had already occurred in the low pressure system.

Figure 1 shows that the common elements of the effects of LBNP and LNP on venous pressure in the intrathoracic region are, in the first place, its marked drop with minimal decompression (to -20, -30 mm Hg) and, in the second place, gradual slowing of changes upon further intensification of decompression, which implies that there are identical mechanisms involved in the effects of these preventive factors on the low pressure system.

Table 1. Parameters of circulation, oxygenation and acid-base equilibrium in mixed venous blood with use of postural factors (control)

Parameters	Orthostatic test	Antiorthostatic test 20°		
		20 min	40 min	60 min
CVP, mm Hg	−2,0±1,0	6,1±0,7*	5,8±0,7*	5,6±0,7*
PPA, mm Hg				
s	11,1±0,9	25,4±1,7*	23,5±1,4*	23,6±1,7*
d	6,1±0,8	13,6±0,7*	12,5±0,8*	12,0±1,1*
m	8,0±1,0	18,2±0,8*	16,5±1,0*	16,2±1,2*
RVF, kg-m/min	0,59±0,1	2,13±0,2*	1,84±0,2*	1,77±0,2*
AP (n=4), mm Hg				
s	113,0±2,2	122,0±2,7	117,0±4,0	119,0±3,2
d	65,3±4,2	65,2±2,1	64,8±2,3	65,8±2,1
m	77,7±1,2	80,3±1,7	78,0±2,9	79,5±2,1
CI, ℓ/min/m²	2,9±0,3	4,4±0,4*	4,1±0,3*	4,1±0,3*
SI, mℓ/m²	33,0±3,0	61,4±4,2*	59,0±3,2*	59,0±3,1*
HR/min	90±4	72±4*	70±3*	71±3*
pH	7,38±0,02	7,38±0,02	7,38±0,02	7,37±0,02
pCO_2, mm Hg	37,8±2	41,4±1,1	41,7±1,1	42,4±1,6
BE, mmole/ℓ	−1,3±1,1	−0,2±0,7	0	0,5±0,7
HbO_2, %	69,3±1,8	76,1±1,0*	75,8±1,0*	75,1±0,9*
C_{O_2}, vol.%	13,3±0,6	14,5±0,4*	14,5±0,4*	14,4±0,4*
AVD_{O_2}, vol.%	5,1±0,3	3,7±0,2*	3,7±0,2*	3,8±0,2*
CU_{O_2}, %	28,0±1,4	20,5±1,0*	20,5±1,1*	20,9±1,1*

Key for this, Tables 2 and 3:

CVP) mean central venous pressure
PPA) pressure in pulmonary artery
RVF) right ventricular function
AP) pressure in radial artery
CI) cardiac index
SI) stroke index
HR) heart rate
BE) base excess
Hb_{O_2}) hemoglobin oxygenation
C_{O_2}) oxygen content
AVD_{O_2}) arteriovenous oxygen difference
CU_{O_2}) oxygen utilization coefficient
s) systolic
d) diastolic
m) mean
*) $P \leqslant 0.05$ (in relation to orthostatic test)

In Figure 2, pressure in the pulmonary artery as a function of degree of decompression is illustrated on a semilogarithmic scale. Analysis of the obtained function revealed that, in the range of LBNP from 0 to -30 mm Hg, the pressure changes in the pulmonary artery can be expressed by the following equation:

$$P^I_{pa} = P_{pa} \cdot e^{\alpha p}$$

where P^I_{pa} and P_{pa} are current and base value of mean pressure in the pulmonary artery (mm Hg), p is the degree of decompression (mm Hg) and α is an exponent that equals 0.035. We took the value of P^I with a 10-15 s lag in relation to p. In the range of -30 to -60 mm Hg, the P^I_{ap} and decompression function is also nonlinear, but it has a more complicated appearance. Perhaps, this reflects involvement of a new mechanism of regulation of pulmonary circulation when decompression is increased to close to -30 mm Hg.

After use of LBNP in mode I for 15-20 min, we observed noticeable changes in parameters of circulation and oxygenation of mixed blood, most values coming close to those recorded in orhtostatic position (Table 2). Further increase in decompression

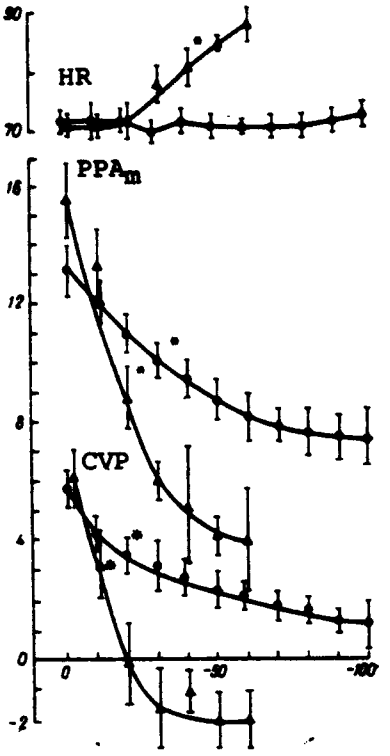

Figure 1.
Dynamics of heart rate (HR), mean pressure in pulmonary artery (PPA_m) and central venous pressure (CVP) under the influence of LBNP and LNP.
Triangles--LBNP, circles--LNP, asterisks--$P<0.05$.

(mode II) was associated with less marked changes; however, pressure in the pulmonary artery and right ventricular function were reliably lower, while arteriovenous oxygen difference and coefficient of utilization thereof were higher than in orthostatic position. It should be noted that with the use of -60 mm Hg LBNP one of the subjects developed a precollaptoid state at the end of the blood-taking procedure, the symptoms of which rapidly disappeared after pressure in the Chibis garment was raised.

Use of LNP in mode I for 15-20 min led to a pressure drop in the right atrium and pulmonary artery; however, like several other circulatory parameters, it remained reliably higher than in orthostatic position (Table 3). Further increase in decompression (mode II) elicited less marked changes in the recorded parameters, while pulmonary artery pressure became virtually the same as in orthostatic position.

With rapid elevation of pressure in the Chibis garment or LNP tube, pressure began to rise rapidly in the right atrium and pulmonary artery, and it soon reached the base level. Moreover, at this level of LNP, the values of these parameters were higher when pressure was equalized to atmospheric pressure than in the presence of decompression. As a result, immediately after decompression they were above levels recorded in the background period (Figure 3). These distinctions were the most apparent with LBNP in the range of -40 mm Hg to 0.

The obtained results indicate that the comparison of LBNP and LNP effects should be drawn with the use chiefly of such parameters as central venous pressure and pressure in the pulmonary artery, since they are highly informative and fundamental to formation of such concepts as pre- and postload on the right ventricle; in addition, they can be precisely recorded quantitatively; they can be measured in both a "stable" state and "transient" period, when negative pressure in the Chibis garment or LNP tube changes rapidly.

The change from orthostatic to head-down position was associated with changes in virtually all parameters of central circulation, particularly pressure in the right atrium and pulmonary artery, which was indicative of an increased load on the right heart. Evidently, a marked increase in pre- and postloads is not indifferent to the myocardium, since it can affect its energetics, oxygen uptake and volumetric coronary blood flow rate [1, 2]. Under such conditions, reduction thereof to the level observed in orthostatic position creates a beneficial situation for myocardial function, since an erect position is more a state of "calm" circulatory homeostasis for man than a stress factor [3]. For this reason, using various preventive factors

to create a situation similar to the one observed in central circulation during the orthostatic test would apparently have a beneficial effect on the myocardium and central hemodynamics as a whole.

Table 2. Parameters of circulation, oxygenation and acid-base equilibrium of mixed venous blood with use of postural factors and various modes of LBNP

Parameters	Orthostatic test	Antiorthostatic test 20°		
		Background	LBNP	
			mode I	mode II
CVP, mm Hg	−1,9±1,0	6,6±0,8*	−0,1±0,7	−1,5±0,6
PPA, mm Hg:				
s	11,6±1,1	22,0±1,5*	11,4±1,0	8,8±0,7*
d	6,8±0,8	11,5±0,9*	5,1±0,6	4,3±0,7*
m	8,4±0,8	16,0±1,3*	7,5±0,7	5,9±0,7*
RVP, kg-m/min	0,65±0,07	1,94±0,3*	0,65±0,1	0,45±0,07*
AP (n=4) mm Hg:				
s	121,0±6,3	124±2,5	116±3,1	113±3,9
d	78,7±1,8	73,7±1,3*	73,0±1,2*	81,0±3,1
m	92,5±3,2	91,0±2,4	86,7±2,1	89±3,0
CI, ℓ/min/m^2	3,0±0,3	4,5±0,4*	3,2±0,3	2,8±0,1
SI, mℓ/m^2	33,2±2,5	65,8±3,9*	43,5±4,6*	31,1±1,7
HR/min	90±3	68±2*	79±3*	92±2
pH	7,4±0,007	7,39±0,004	7,40±0,006	7,40±0,005
pCO_2, mm Hg	38,2±2,3	40,4±2,0	39,6±2,3	38,7±2,0
BE, mmole/ℓ	−0,3±1,5	1,1±1,2	0,3±1,7	−1,0±1,1
Hbo_2, %	65,6±1,6	72,5±1,2*	65,3±1,2	61,4±1,5*
Co_2, vol.%	12,6±0,4	13,9±0,4*	12,5±0,3	11,8±0,3*
$AVDo_2$, vol.%	5,7±0,3	4,4±0,2*	5,8±0,3	6,5±0,3*
CU_{O_2}, %	31,1±1,6	24,1±1,0*	31,4±1,3	35,7±1,6*

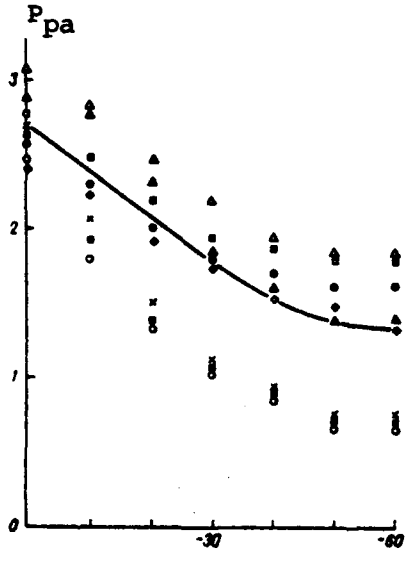

Figure 2. Logarithm of mean pulmonary artery pressure as a function of LBNP level. Explanation given in the text. The symbols refer to individual changes in the parameters.

LBNP and LNP raised transmural pressure in vessels of the corresponding regions, and this is apparently observed in superficial veins. In turn, elevation of transmural pressure leads to increase in capacity of the vascular system and subsequent increase in volume of blood in it as a result of a corresponding decline of its central volume. Since changes in central venous pressure and circulating blood volume (as well as pressure in the pulmonary artery--blood volume in the lungs) are related, to some extent, as a virtually linear function, the redistribution of blood in vessels of the lower extremity would be associated with corresponding changes in these parameters [4, 5].

For this reason, it is not surprising that essentially the same patterns were inherent in the curves we obtained as for the classical curve for the venous capacity--transmural pressure function. Evidently, the change

in central venous pressure and pulmonary artery pressure can be interpreted as an indirect indicator of changes in vein capacity in the region of decompression. If this is so, the curves we obtained (from the base level to virtually a plateau) could also reflect the phases of change in capacity of veins. However, this hypothesis must be checked, with concurrent recording of pressure in the intrathoracic region and vein capacity in the decompression region.

Table 3. Parameters of circulation, oxygenation and acid-base equilibrium of mixed venous blood with use of postural factors and different modes of LNP

Parameters	Orthostatic test	Antiorthostatic test 20°		
		background	LNP	
			mode I	mode II
CVP, mm Hg	—2,7±0,8	5,6±0,87*	3,4±0,3*	2,0±0,2*
PPA, mm Hg:				
s	11,1±0,6	20,4±1,4*	15,8±1,0*	13,1±0,8
d	6,1±0,7	9,9±1,0*	6,6±0,7	5,6±0,5
m	8,0±0,6	13,9±1,3*	10,2±0,7*	8,4±0,6
RVF, kg-m/min	0,6±0,07	1,6±0,18*	1,0±0,09*	0,8±0,07*
CI, ℓ/min/m²	2,9±0,3	4,0±0,2*	3,8±0,2*	3,4±0,1*
SI, mℓ/m²	32,0±3,2	60,7±1,4*	56,0±2,6*	50,8±1,7*
HR/min	90±2,6	66±2,1*	67±1,8*	69±2,0*
pH	7,38±	7,39±	7,40±	7,39±
pCO_2, mm Hg	41,6±0,6	40,8±1,1	39,8±1,6	38,2±1,8
BE, mM/ℓ	—0,52±0,8	—0,58±0,9	—0,59±0,9	—1,74±0,95
Hbo_2, %	67,3±1,1	72,7±1,3*	71,4±1,0*	70,3±1,2
Co_2, vol.%	12,7±0,33	13,7±0,48*	13,5±0,44*	13,4±0,41*
$AVDo_2$, vol.%	5,6±0,27	4,2±0,17*	4,5±0,14*	4,7±0,17*
CUo_2, %	30,4±0,9	23,7±1,1*	25,1±0,9*	26,3±1,13*

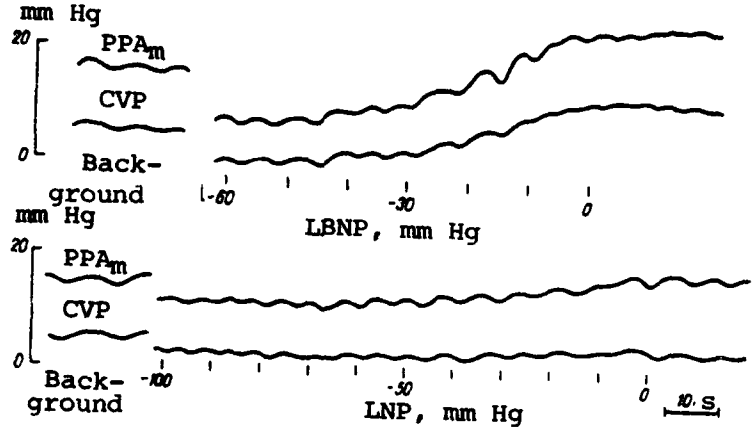

Figure 3. Changes in mean pressure in pulmonary artery (PPA_m) and central venous pressure (CVP) recorded on one of the subjects during "dumping" of pressure in Chibis garment and LNP bag

The most marked changes in the parameters were demonstrated with a mild degree of decompression, and further increase thereof was associated with less marked changes. The results obtained conform well with data in the literature [6, 7]. In particular,

Zoller et al. [7] demonstrated that central venous pressure dropped by 42, 59, 74 and 93% in the LBNP range of -5, -10, -20 and -40 mm Hg, respectively. As we have demonstrated, such changes were inherent not only in central venous pressure, but pressure in the pulmonary artery. Apparently, low levels of LBNP or LNP decompression are sufficient to stimulate the receptors of the low pressure (cardiopulmonary) system, whereas stimulation of high pressure receptors (sinoaortic) is possible, if we consider the reaction of pulse rate and arterial pressure, only with high levels of LBNP [8].

This distinction (marked changes in the low pressure system with low levels of decompression) is apparently attributable to a change in vein capacity in the area affected by LBNP. It is known that their volume increases drastically with mild elevation of transmural pressure (to about 30 mm Hg), and further elevation thereof is associated with less noticeable changes in capacity. In particular, a study of the LNP level--lower leg volume function revealed that this volume increases by about 5% with LNP of 0 to -50 mm Hg, whereas it only increases by 2% with further lowering of pressure to -100 mm Hg [9]. It is generally believed that changes in vein capacity with minimal elevation of transmural pressure are due essentially to the passive component (change in geometry of their lumen) and changes in actual elasticity occur with greater decompression, playing a less appreciable role in elastic function. On the basis of these conceptions, it becomes clear why the base transmural pressure in the region of decompression is one of the important factors that affect the reaction of central circulation to preventive factors.

The effect of negative pressure on central circulation depends not only on the degree of decompression and base transmural pressure, but on area and region of decompression [10]. Evidently, expressly this explains the various quantitative changes in parameters with use of LBNP and LNP, which were demonstrated both in the "transitional" period and in a "stable" state. Moreover, elasticity of vessels of the lower leg and foot, which are subject to significant changes in transmural pressure with ordinary postural factors, differs from elasticity of vessels in overlying regions.

Interestingly enough, with the same level of LBNP, central venous pressure and pressure in the pulmonary artery during equalization of pressure to atmospheric level were higher than when pressure was lowered in the tube. The main cause of this is, apparently, the fact that volumetric blood flow rate may have a considerable influence on the vein capacity -- transmural pressure ratio. We know that when transmural pressure is the same the capacity of veins is smaller when blood flow is faster [11]. In other words, when LBNP is "dumped," when blood flow increases, the vein capacity with a given transmural pressure may be lower than with increase in decompression. This results in shifting of a larger volume to the intrathoracic region and subsequent, more marked increase in central venous pressure and pulmonary artery pressure.

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USE OF NUTRIENTS TO CORRECT THE ADRENOCORTICAL SYSTEM

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 21 Nov 80) pp 19-22

[Article by S. Kalandarov, V. P. Bychkov, I. D. Frenkel' and T. P. Petukhova]

[English abstract from source] Two 60-day studies in which 10 healthy volunteers participated were carried out. In both studies stress situations were simulated by a chamber rise to an altitude of 8000 m, anticipation of exposure to acceleration, and psychological tests. The changes found were dependent on both the type of the stressor applied and duration of the exposure. Nutrient supplements did not influence the adrenocortical function of the adrenals.

[Text] At the present time nervous-emotional stress is drawing the attention of many researchers, since it has great practical implications because of expansion of the range of occupations that require flawless function of all of the body's systems in the presence of nervous-emotional tension [1, 2]. We have explored in this study the possibility of using nutrients to correct changes in functional state of the adrenosympathetic system and adrenal cortex of man in a state of nervous-emotional stress.

Methods

The data were obtained from two 60-day tests involving 10 healthy male subjects (5 men in each study) ranging in age from 23 to 41 years. In both studies, we used simulated ascent to an altitude of 8000 m in a pressure chamber, anticipation of accelerations on a centrifuge and a psychological test (performance of tasks differing in difficulty within a limited time period) to simulate stress situations. The interval between exposure to these factors constituted 15 days [3].

The diet consisted of canned and dehydrated foodstuffs; it was balanced with respect to levels of main constituents and had a caloric value of about 3000 kcal/day.

Food supplements were used in addition to the allowance in the second study for correction of metabolic changes and to maintain a high level of work capacity in the presence of stress. We used three variants of food supplements, which included different combinations of vitamins (ascorbic acid, Undevit multiple vitamins and vitamin B_{15}), minerals (potassium, phosphorus, magnesiums, chlorides, calcium), glucose and phosphatide concentrate. The choice of these supplements was based on data in the literature [4, 5], which were indicative of higher requirements in the

Table 1. CA (μg) and 17-HCS (mg) levels in 24-h urine before and after stress factors (M±m)

Study	Parameter	Background	Simulated climb in chamber			Anticipation of centrif.		Psychological test		
			before	during	after	before	during	after	before	during	after
I	E	4,9±0,57	4,7±0,87	4,2±0,66	5,1±0,65	5,1±0,42	4,9±0,57	5,5±0,67	4,2±0,57	4,7±0,57	3,6±0,46
	NE	13,1±1,12	15,3±1,02	14,3±1,58	12,6±0,6	14,4±0,9	17,0±2,0	14,3±1,6	15,9±2,4	16,4±2,0	11,3±1,1
	DA	265,9±19,19	297,7±45,5	230,8±25,3	273,4±19,1	268,4±15,7	304,4±39,6	316,0±34,7	299,4±36,3	263,0±39,4	192,2±19,8
	Dopa	26,3±1,01	24,0±4,4	21,8±2,94	25,6±3,2	27,3±2,37	31,4±1,97	25,6±3,78	29,2±3,54	24,7±2,88	20,7±1,31
	17-HCS	6,8±0,39	9,5±0,23	10,6±0,36	9,1±0,26	9,2±0,7	7,8±0,66	7,7±0,46	7,7±0,65	8,6±0,31	6,8±0,26
II	E	4,3±0,4	3,9±0,66	3,9±0,72	3,8±0,9	3,9±0,35	3,8±0,4	4,0±0,45	1,3±0,33	3,3±0,7	3,0±0,6
	NE	11,2±1,01	9,6±1,05	9,7±1,32	9,7±2,2	14,1±1,09	13,7±0,92	12,8±0,96	5,1±1,0	9,2±1,1	8,4±1,3
	DA	254,8±20,8	214,9±18,3	208,1±9,3	202,2±16,3	275,7±26,8	264,5±8,0	230,1±11,7	202,2±17,1	256,4±49,7	238,1±32,4
	Dopa	27,4±1,5	25,1±4,4	24,2±2,2	21,1±2,34	25,6±2,7	24,9±2,4	25,2±4,1	17,6±1,9	34,8±4,06	31,6±5,4
	17-HCS	5,7±0,4	11,6±1,73	11,5±1,24	6,0±0,44	6,7±0,53	6,2±0,32	7,7±0,88	6,9±1,21	8,0±0,9	8,4±1,74

presence of nervous-emotional tension. The subjects were given food supplements for 5 days: on the day before and day of use of each of the stress factors [3].

Functional state of the adrenosympathetic system was assessed on the basis of catecholamine (CA) excretion, which was assayed in 24-h urine specimens by the method of E. Sh. Matlina et al. [6]. To evaluate adrenocortical function, we assayed 17-hydroxycorticosteroids (17-HCS) in 24-h urine by the method of Reddy-Brown [7, 8] and 11-hydroxycorticosteroids (11-HCS) in blood plasma (total, protein-bound and free). We used the method of DeMoor et al. [9] as modified by L. V. Pavlikhina et al. [10] for separate assays of protein-bound and free forms of 11-HCS in plasma. The fluorimetric method of DeMoor et al. [11] as modified by Yu. A. Pankov and I. Ya. Usvatova [12] was used for quantitative assays of total 11-HCS and fractions thereof.

Results and Discussion

In the first study, all three variants of stress situations had no appreciable effect on CA excretion in urine. As can be seen in Table 1, there were unreliable differences in CA levels in urine throughout the period of this study. We only observed one decline of dopamine (DA) ($P<0,02$) and dopa ($P<0.05$) levels in the aftereffect period following the psychological test.

In the second study, on the eve of the psychological test (before using stress factor) we observed a decrease in excretion of epinephrine (E) and norepinephrine (NE; $P<0.01$) and biological precursors thereof--dopa ($P<0.01$ and DA ($P<0.05$) in urine. At other terms, the parameters studied differed little from background levels.

Table 1 also shows that, with simulation of ascent in pressure chamber in study I, the 24-h level of excretion of 17-HCS in urine was elevated at all times, as compared to background data. The highest 17-HCS level was demonstrated on the day of exposure to this factor ($P<0.001$). The amount of free 11-HCS diminished somewhat, while the bound

form showed an increase (Table 2). During anticipation of centrifuging, the concentration of 17-HCS in urine was elevated in the subjects on the day before use of this factor ($P<0.05$). We also observed some increase in blood plasma levels of both free and protein-bound forms of 11-HCS (see Table 2). An increase in 17-HCS was also observed on the day of the psychological test ($P<0.02$). Concurrently, there was a decrease in concentrations of all forms of hormones in blood (see Table 2).

Table 2. Levels of total, protein-bound and free forms of 11-HCS before and after use of stress factors (M±m)

Study	Stress factor	11-HCS					
		total		protein-bound		free	
		before	after	before	after	before	after
I	Background	16,7±1,1	—	15.5±0,9	—	1,3±0,3	—
	Climb in pressure chamber	16,8±1,2	17,2±0,94	15,4±0,9	16.3±1,06	1,4±0,29	0,9±0,47
	Anticipation of centrifuge	18,9±0,72	18,9±0,72	17,2±0.00	17,2±0,00	1,7±0,72	1.7±0,72
	Psychological test	15,4±0,57	14,3±0,5	15,0±0,7	13,7±0,26	0.4±0,28	0,6±0,26
II	Background	13,8±1,5	—	12,6±0,9	—	1,2±0,9	—
	Climb in press. chamber	12,7±0,8	12,1±0.9	11,9±0,7	11,1±0,9	0,7±0,04	1,0±0,6
	Anticipation of centrif.	11,5±1,1	13,7±1,8	11,0±0,7	12,3±0,7	0.6±0,03	1,4±0,8
	Psychological test	12,7±0,06	11,7±1,0	.:,3±0,8	10,7±1,4	0,4±0,87	1,0±0,04

In study II, elevated 17-HCS levels in urine were observed 1 day before simulation of ascent in pressure chamber, on the day of the "climb" and on the day of the psychological test ($P<0.05$). Table 2 shows that none of the stress factors used against the background of intake of food supplements had an effect on levels of free and protein-bound forms of 11-HCS in blood plasma.

According to the data of Blaschko [13], the amino acids, phenylalanine and tyrosine, are the base products for CA synthesis. CA precursors (dopa and DA) are formed from these animo acids by means of decarboxylation.

Evidently, with the use of a stress factor, in particular the psychological test, the enzyme system which regulates CA synthesis (phenylalanine-4-hydroxylase and tyrosine-β-hydroxylase) is inhibited. The data of T. F. Vlasova, which are indicative of elevation of phenylalanine level (from 0.73±0.04 to 1.05±0.03 mg%; $P<0.001$) and tyrosine (from 0.80±0.05 to 1.08±0.09 mg%; $P<0.05$) in the presence of emotional stress, can serve as indirect evidence of diminished activity of this enzymatic system.

The attenuated reaction of the adrenosympathetic system to the psychological test could be attributed not only to diminished activity of the enzymatic system, but increased CA catabolism [14], as well as increased tissular sensitivity to them [15].

In study I, we observed changes in adrenocortical function under the influence of the stress situations. Simulation of a climb in the pressure chamber and anticipation of centrifuging elicited increase in adrenocortical function, while the psychological test, on the contrary, elicited some decrease.

Analogous changes were observed by A. A. Viru [16] and A. Ya. Soosaar [17]. It may be assumed that the psychological tests caused increased utilization of corticosteroids by different tissues [18], which led to a decrease in concentration thereof in blood.

Thus, the results of these studies revealed that the nature of the demonstrated changes depended both on the type of stress factor used and duration of exposure to it. Intake of food supplements had no appreciable effect on adrenocortical function of the adrenals.

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ECHOVENTRICULOMETRY USED TO STUDY SPINAL FLUID CIRCULATION DURING REDISTRIBUTION OF FLUIDS IN A CRANIAL DIRECTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 31 Jul 80) pp 22-23

[Article by V. I. Sokolov]

[Text] Evaluation of the functional and adaptive mechanisms of the system, which are involved in maintaining cerebral hemodynamics and dynamics of spinal fluid when there is redistribution of fluids in a cranial direction due to absence of hydrostatic pressure [1] is one of the pressing problems in the study of man's acute adaptation to weightlessness. The extreme variability of symptoms and differences in time of man's adaptation to weightlessness are indicative of the dissimilar degree of development of these mechanisms. If development thereof is poor, there may be an increase in venous blood in the skull with subsequent development of circulatory hypoxia [2]. Studies of mechanisms of compensation for delivery of blood to the brain revealed the importance of metabolic acidosis, which leads to dilation of precapillaries and creates conditions for adequate circulation of blood [3]. However, the role of spinal fluid in regulating increased delivery of blood to the cranial cavity is still unclear, although it is a hydrodynamic medium that occupies 10% of the entire capacity of the skull. Moreover, spinal fluid pressure, together with pressure in intracerebral veins, is a factor that determines resistance to arteriolar blood flow and, consequently, could play a substantial role in intracellular metabolic disorders.

We shall discuss here the possibility of evaluating intracranial spinal fluid pressure by the method of echoventriculometry, which is widely used in clinical practice for diagnostication and determination of severity of the hypertensive syndrome [4].

Methods

Echoventriculometry is based on delivery to the brain of short ultrasonic pulses at a frequency of 0.88 and 1.76 MHz and reception of signals reflected from its internal structures. The rate of propagation of ultrasonic waves was 3500 m/s in cranial bones and 1500 m/s in brain matter. Ultrasound has the capacity of being refracted on the boundary of media differing in acoustical resistance, which served as the basis of echoventriculometry.

To examine the ventricular system of the brain, the ultrasonic probe must be situated in the central temporal lead, since with such localization the signal is

formed by the third ventricle (Figure, A) and it is possible to determine the size of the latter with a 2.5% error margin, the lateral ventricles being in the probe's dead space and demonstrable only with increase in cerebrospinal pressure.

Position of ultrasonic sensor (A) and echogram in central bitemporal lead (B)
a) central temporal lead
HK, KK) first and last complexes

To pinpoint the third ventricle, a transmission mode is used, where one probe emits ultrasonic waves and the other receives them; to determine the dimensions of cerebral ventricles, the emission method is used, where the ultrasound source is used also as the receiver of energy reflected from the tissular interface.

To assess the degree of dilatation of the ventricular system of the brain when there is impaired circulation of cerebrospinal fluid as the cause of elevation of intracranial pressure, the following indexes were elaborated (Figure, B): index Dv_i of the third ventricle (ratio of doubled transmission to size of third ventricle), a reduction of which is indicative of dilation of cerebrospinal fluid tract and, as a rule, an early diagnostic sign of elevation of spinal fluid tension; Pm_i, index of the medial wall (ratio of magnitude of transmission to distance between the M echo and medial wall of the lateral ventricle), increase of which is indicative of significant dilatation of the third ventricle and lateral ventricle, i.e., marked impairment of cerebrospinal circulation and elevation of intracranial pressure.

The EES-12 instrument was used to evaluate this method's capabilities in model studies.

Results and Discussion

This study was conducted with the participation of 20 male subjects 23 to 32 years of age (mean age 28 years), who were submitted once to an antiorthostatic [head-down tilt] test (-30°) for 30 min. Clinically, the subjects presented puffiness and hyperemia of the face, congested nose and hoarse voice, indicative of redistribution of blood in a cranial direction. The subjects complained of heaviness of the head, headache, microphotopsia, illusion of overturned body or rocking, which were indicative of changes in the vertebrobasilar system. Seven subjects showed elevation of intracranial pressure due to fluid pressure, without signs of edema of cerebral tissue, which conformed well with the clinical signs of endurance of head-down position. In addition to signs of venous stasis, the subjects reported splitting headaches, illusion of overturned body, rocking and mild nausea.

The subjects were divided into two groups: the first consisted of individuals (7) who presented enlargement of cerebral ventricles with extreme variability of symptoms; the second consisted of those (13 men) who did not present this phenomenon.

The cerebrospinal pressure was low (Dv_i = 23.1+0.4, $P<0.0003$) in the initial horizontal position of subjects in the second group, whereas this index was higher in the first group (Dv_i = 20.9±0.1, $P<0.0003$), which could be evaluated as a certain predisposition for development of the hypertensive syndrome. In the first minute of head-down position, both groups of subjects presented a decline of the index

of the third ventricle: to 15.8±0.2 ($P<0.0003$) in the first group and 16.5±0.1 ($P<0.0003$) in the second. This was indicative of elevation of cerebrospinal pressure, apparently due to hydrodynamic flow of fluid into the cranial cavity. In the 10th min, the first group of subjects presented enlargement of lateral ventricles of the brain (Pm_i = 7.8±0.4, $P<0.005$) and dilated third ventricle (Dv_i = 15.4±0.3, $P<0.0003$), which could be attributed to increase in spinal fluid component of intracranial pressure. The changes persisted to the 30th min and increased gradually (Pm_i = 8.3±0.2, $P<0.005$). In the second group, we observed increase of Dv_i to 22.0±0.2 ($P<0.0003$), which could be evaluated as compensatory elevation of cerebrospinal tension with redistribution of fluids in a cranial direction. When the subjects switched to horizontal position, there was an increase in index for the third ventricle to 19.4±0.2 ($P<0.0003$) in the first group, i.e., to a level that was still lower than base spinal pressure, whereas in the second group of subjects this parameter was close to the background value (Dv_i = 24.4±0.1, $P<0.0003$). The latter should be interpreted as compensatory flow of spinal fluid in a caudal direction. Restoration of base level of spinal pressure occurred by the 15th min in the first group of subjects, which was indicative of inadequacy of compensatory mechanisms of cerebrospinal pressure.

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EFFECT OF ONE-DAY IMMERSION ON CARDIORESPIRATORY PARAMETERS OF MAN DURING EXERCISE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 4 Jan 81) pp 24-26

[Article by S. M. Belyayev]

[English abstract from source] The effect of 1-day water immersion ("dry" immersion) on cardiorespiratory parameters of test subjects performing submaximal exercises was studied. Individual changes involving increases in heart rate and cardiac load index, and decreases in oxygen pulse and systolic volume were seen. They suggest a decline of adaptive ability of the human body to muscular loads after 1-day water immersion.

[Text] It is known that cosmonauts present functional deviations referable to the cardiovascular and other systems in the very first hours of flight [1-3]. Our objective here was to assess some of the reactions of the human cardiorespiratory system in response to graded exercise during adaptation to simulated weightlessness lasting 1 day.

Methods

The studies were conducted on 8 healthy male subjects 25-32 years of age. We used immersion in water (method of "dry" submersion [4]) for 24 h as a model of weightlessness. The subjects were kept on the usual food allowance. Pedaling on a bicycle ergometer at the rate of 600 kg-m/min for 15 min served as the functional test, which the subjects performed in supine position. Pedaling rate constituted 65±5 r/min.

Before the test, during the 8th and 15th min thereof, we determined the following: O_2 uptake ($\dot{V}_{O_2}$) and CO_2 output, for which purpose exhaled air was collected in 100-ℓ Douglas bags (gas analyzers were used for analysis); minute respiratory volume ($\dot{V}$) using a GCB-400 gas counter, minute cardiac volume (MV) by the method of CO_2 rebreathing followed by calculations according to Defares [5]. The subjects breathed a gas mixture consisting of 4% CO_2 in O_2 (respiratory rate of 45/min) for 10 s in order to rule out recirculation of blood. CO_2 tension in the last batch of exhaled air (according to capnogram) was compared [or equated] to CO_2 content of arterial blood.

Systolic and diastolic arterial pressure (AP) were measured by the tachooscillographic method using an AD-KTs type instrument at rest, in the 8th and 15th min of exercise, as well as 3d and 7th min after stopping exercise.

Some cardiorespiratory parameters during pedaling on bicycle ergometer (M±m)

Stage of test	V_{O_2}, ml/kg·min		OP, ml/beat		MV, l		SVH, ml		HR/min	
	before immersion	during immersion	before immersion	during immersion	before immersion	during immersion	before immersion	during immersion	before immersion	during immersion
At rest	2,2±03	2,3±0,3	3,4±0,7	3,1±0,6	3,48±0,27	4,16±0,29	65,3±8,6	70,0±6,5	55±3	59±2
8th min of exercise	20,5±2,6	20,4±2,1	12,2±0,7	11,5±0,7	19,13±1,38	17,12±1,36	149,9±10,4	127,3±16,3	130±5	136±6
12th min of exercise	21,3±2,6	21,0±2,3	12,3±1,1	10,3±0,6	16,78±1,00	17,49±0,88	127,6±5,0	120,2±9,8	132±5	147±4
										$P<0,05$

Key: MV--minute volume

We recorded the EEG in the Neba leads during the entire test period. We estimated oxygen pulse (OP), systolic volume of the heart (SVH), coefficient of oxygen utilization (CU_{O_2}) and cardiac load index [6].

We conducted the tests at the same time of day, in the mornings, under basal metabolic conditions. Background recordings were taken 24 h before submersion in an immersion tank, after the subject had spent 1 h in horizontal position. The tests started 10-15 min after immersion, and the subjects were not allowed to move from horizontal position. In the background period and during immersion, we determined the 24-h fluid balance as the difference between fluid intake and diuresis.*

The data were submitted to statistical processing with the use of Student's criterion.

Results and Discussion

All of the subjects performed the exercises with relative ease prior to immersion. The dynamics of changes ($\dot{V}_{O_2}$) and heart rate (HR) were indicative of their reaching a "stable state" [7] (see Table). The MV changes were undulant, with maximum values in the middle of the exercise period, in the 8th min, and gradual decline by the 15th min. Such MV dynamics reflect changes in SVH, which decreased by 14.9% by the end of the test, as compared to the 8th min of exercise.

After 1-day immersion, parameters $\dot{V}_{O_2}$ and $\dot{V}$ at rest in horizontal position did not undergo appreciable changes. We observed an increase in HR (by 7.3%), SVH (by 7.2%) and decline of OP (8.8%); MV increased by 19.5%. Yu. D. Pometov [8] demonstrated analogous changes in the cardiovascular system, and in his studies MV increased by 23.5% and 24.4% after 8 and 22 h of immersion, respectively. Such changes in circulatory volumes reflect redistribution ot fluids to the upper half of the body due to compensation by the water environment of hydrostatic force of blood.

*Fluid balance data were kindly provided by Ye. A. Aleksandrova.

After immersion, there was negligible increase in HR (by 4.6%) in the 8th min of the test. OP decreased by 5.7%, MV decreased by 0.5% and SVC by 15.1%. Parameters CU_{O_2} and $\dot{V}_{O_2}$ did not change. Two subjects presented a 15.6% elevation of systolic AP, and the others a 10.3% drop. There was virtually no change in diastolic AP. The cardiac load index (which serves as an indirect indication of myocardial oxygen uptake [6]) was 6.4% above the background value. Further exercising after immersion led to marked changes in the cardiovascular system. In the 15th min of exercise, there was a statistically reliable increase in HR (by 11.4%, $P<0.05$). MV increased by 4.2% due to the HR increment, since SVC decreased by 5.8%. We demonstrated a mean 10.2% drop of AP (systolic) in 2 subjects, whereas in the others (the group that also included individuals with elevated systolic AP in the 8th min of exercise) it rose by a mean of 12%. Diastolic AP did not change, as was the case in the middle of the exercise period. The cardiac load index was 14% above the background level. Parameters $\dot{V}$ and $\dot{V}_{O_2}$ did not undergo appreciable change. OP dropped by 16.3%. Similar changes in HR and SVH were demonstrated in crew members of the Soyuz series of spacecraft during exercise [1].

Before immersion, the subjects reached virtually a "stable state" [7] during exercise, whereas after immersion in the tank the heart rate continued to increase with such exercise.

In the 3d min of the aftereffect period following immersion HR was 6.7% higher than the background level. This warrants the assumption that there was some degree of deconditioning, which developed as a result of 1-day immersion. In the 7th min of the aftereffect period there was no difference between HR before and after immersion.

During the day spent in immersion, we observed increased renal excretion of fluid, which constituted a mean of 823 mℓ (with individual fluctuations from 48 to 1333 mℓ). In the background period, the difference between fluid intake and diuresis was more moderate, constituting a mean of 226 mℓ/day. We failed to demonstrate a correlation between 24-h fluid balance and changes in physical work capacity.

The results of these studies revealed that 24-h immersion in water elicited appreciable changes in the cardiovascular system, which were indicative of decline of reserve capabilities of the body in response to physical exercise. The decline of SVH during moderate exercise suggests that there is a decrease in contractile capacity of the myocardium [9]. The increase in HR and cardiac load index proves that there was an increase in energy expended by the heart for the same load. The decline of OP characterizes a decrease in effect of adaptation of the cardiorespiratory system after 1 day of immersion. The observed decrease in reserve capabilities of the circulatory system during exercise following immersion was characterized by individually marked reactions, which it is expedient to take into consideration when using measures to enhance man's physical work capacity.

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EFFECT OF HYPOKINESIA IN HEAD-DOWN POSITION ON MAN'S EQUILIBRIUM FUNCTION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 26 Sep 80) pp 26-29

[Article by A. R. Kotovskaya, L. N. Gavrilova and R. R. Galle]

[English abstract from source] Six test subjects who participated in 182-day head-down study at -4° were examined stabilographically before and during the test. During the first 30 days they showed impaired equilibrium which later was relatively stabilized. Continuation of the bed rest study did not impair drastically stability of upright standing. It was shown that the contribution of optic sensors into the recovery of the equilibrium function increased during the second half of the bed rest study. Provocative tests suggest that bed rest related impairment of equilibrium occurs due to vestibular changes and deconditioning.

[Text] Virtually all cosmonauts presented some changes in equilibrium after completion of space flights [1, 2]. The main cause of such disturbances is believed to be their long-term exposure to weightlessnes and the related lack of sensation of the customary support and gravity acting along the body's longitudinal axis. Much significance is attributed to functional changes in sensory systems involved in regulation of erect position [3-5].

However, the methodological difficulty of studying equilibrium during a space flight and, to some extent, after the cosmonauts landed did not permit exact evaluation of the significance of the functional changes to disturbances of postural equilibrium.

To date, considerable data have been accumulated indicative of onset of equilibrium disturbances under the influence of hypokinesia of varying duration [6-8]. It must be stressed that these studies were conducted only after termination of hypokinesia, i.e., in essence the changes in equilibrium function were investigated only in the recovery period. At the same time, it is important to conduct dynamic studies of equilibrium function during hypokinesia in order to comprehend the patterns and mechanisms of development of equilibrium disorders, which could be of practical value to elaboration of methods for prevention thereof following space flights.

Our objective here was to study the dynamics of changes in postural equilibrium during long-term hypokinesia and to determine the role of visual, vestibular and proprioceptive stimulation in these changes.

Methods

This investigation involved hypokinesia for 182 days, with the subjects in antiorthostatic position, the head end of the bed being tilted down at an angle of -4°.

Six essentially healthy men 35-40 years of age participated in the tests.

Stabilography [9] was used to assess the ability to maintain equilibrium in vertical position. The subjects were examined twice in the background period and 7 times during hypokinesia: on the 4th, 14th, 30th, 50th, 90th, 134th and 182d days. The subject stood on a sensitive ["perceiving"] platform with his eyes open, "at attention" with the feet pointing out at an angle of 45° for stabilography. We used closed eyes, change in sensation of support (by using a porolon [plastic] mat 100 mm thick), circular head movements (10 active rotations in 20 s) as additional functional tests to make it more difficult to retain equilibrium. We examined well-being while standing on the stabilographic platform, frequency and amplitude characteristics of the stabilograms. In this report, we submit data on vacillation of the body in the frontal plane. The data were submitted to statistical processing.

Results and Discussion

In the background period, the subjects did not present any subjective reactions to equilibrium tests. The results of the background stabilographic studies (5 days before the start of the main study) are illustrated in Figure 1.

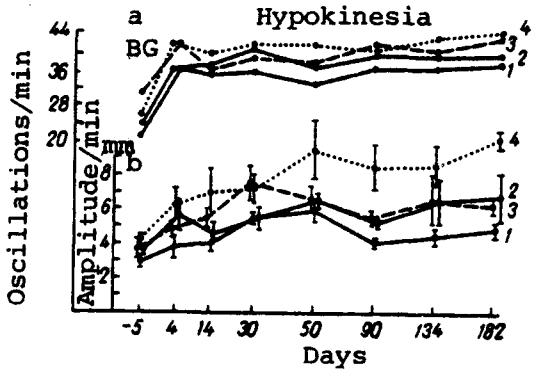

Figure 1.
Stabilographic parameters in the course of 182-day hypokinesia
1) eyes open BG) background
2) eyes shut
3) standing on porolon mat
4) test with circular head movements
X-axis, day of study; y-axis:
a) number of vacillations
b) amplitude of vacillations

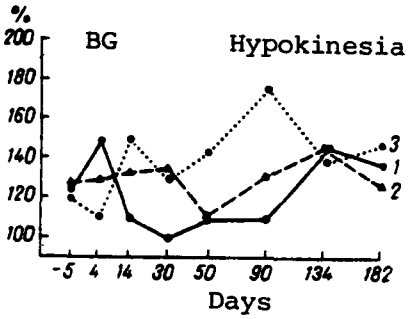

Figure 2.
Correlation between amplitude parameters of stabilogram (%) during functional tests in the course of 182-day hypokinesia
1) standing with eyes open and shut
2) standing with eyes open on soft and firm surface
3) eyes shut in test with and without circular head movements

As can be seen in Figure 1, exclusion of visual monitoring led to an increase in frequency and amplitude parameters by 14 and 24%. After the test with circular head movements, the amplitude of vacillation of the body's general center increased by 20% and frequency increased by 80%. The change in afferentation from the foot

region (to obtain this effect the subject stood on a soft surface--a porolon mat) also affected stability. The frequency and amplitude parameters increased by 50 and 27%, respectively. Thus, background stabilography revealed that the test using a soft support (standing on porolon mat) had the most marked adverse effect on equilibrium and the test with circular head movements and the least marked effect. These data, which were tested on many people, served as the basis for analysis of changes in postural equilibrium under hypokinetic conditions [10].

Throughout the 182-day period of hypokinesia, changes in well-being occurred during the stabilographic tests. For the first 30 days, there were complaings of brief pain in the gastrocnemius, general weakness, vertigo and "sensation of rocking on waves," which increased in both severity and diversity of symptoms. The subjective symptoms during stabilographic tests became stable between the 30th and 182d day.

The number of vacillations of the general center of gravity, determined from the stabilograms, changed insignificantly over the entire period of hypokinesia (from 33-41 oscillations per min; see Figure 1a).

The amplitude of vacillation of the general center of gravity in the frontal plane when standing on a hard surface increased unreliably (by no more than 24%) in the first 14 days of hypokinesia, as compared to background data. Testing on the 30th day of hypokinesia revealed a 93% increase in amplitude, and this was statistically reliable in comparison to base values. From this day to the end of the hypokinetic period, there were insignificant changes in stabilogram amplitude, as compared to the 30th day, with some tendency toward decline (see Figure 1b, curve 1).

With exclusion of vision, the amplitude of vacillation increased significantly. Thus, it constituted 160% of the base value with eyes shut on the 30th day. Thereafter, we failed to observe appreciable changes in amplitude of vacillation with the eyes closed; however, there was some tendency toward increase thereof (see Figure 1b, curve 2).

During hypokinesia, standing on a soft surface (porolon mat) was associated with an increase in stabilogram amplitude. The greatest increase was observed on the 30th day (by more than 100%). Thereafter, it decreased, but vacillation amplitude remained higher by 70-80% than the base values up to the end of the hypokinetic period (Figure 1b, curve 3).

The test with circular head movements had a stronger effect on stability in erect position. This functional test, which is addressed primarily to the vestibular system, elicited a reliable 70-150% increase in amplitude of vacillations of the body starting on the 14th day of hypokinesia (see Figure 1b, curve 4).

Thus, these data are indicative of progressive worsening of equilibrium function during the first 30-50 days of antiorthostatic hypokinesia with subsequent relative stabilization of vacillation amplitude. However, after 50 days, we observed some tendency toward attenuation of equilibrium disturbances with the subjects standing on firm and soft surfaces. At the same time, with the eyes shut we observed a tendency toward further increase in amplitude. These tendencies could not fail to affect the correlation between amplitude parameters of the stabilogram, which characterize involvement of vision, proprioception and the vestibular system in regulation of an erect position.

Figure 2 illustrates the percentile correlations of stabilogram amplitude parameters with the subjects standing with the eyes closed and open, with the eyes open on soft and hard surfaces, with the eyes shut for the test with and without circular head movements. These correlations reflect the direct involvement of vision, proprioception and vestibular system in holding an erect position.

As we see, during hypokinesia there was a change in correlation between amplitude parameters of the stabilogram when standing with the eyes open and closed. While it constituted 124% in the background studies, it decreased to 100-114% between the 14th and 90th day, then increased to 140% between the 134th and 182d day (see Figure 2, curve 1). Consequently, it can be considered that there was a change in involvement of the visual analyzer in holding the erect position: during the first half of the hypokinetic period, the role of vision in regulation of position diminished substantially and during the second half (particularly after the 134th day) it increased, as compared to base data.

The influence of changes in efferentation from the foot region was less noticeable. The correlation between amplitudes when standing on soft and hard surfaces diminished on the 50th day and increased on the 134th, remaining at the level of base values at other times (see Figure 2, curve 2).

The influence of circular head movements on stability of standing increased by the 14th day and reached a maximum on the 90th day of hypokinesia (see Figure 2, curve 3). The results of the test with circular head movements confirmed the opinion of some researchers [11, 12] that there is deconditioning of the vestibular system under hypokinetic conditions, and they are indicative of considerable impairment of equilibrium function under the influence of this minimal vestibular test, which is very common in everyday life.

In addition, Figure 2 shows that there was a change in effects of various functional tests on stability in erect position, as compared to background levels. During hypokinesia, maximum disturbances occurred under the influence of vestibular loads and minimum ones with the eyes closed.

Thus, we observed certain changes in equilibrium function in the course of long-term (182 days) hypokinesia. The results of this study enalrge upon data in the literature [5-8] concerning the effect of hypokinesia on capacity to maintain equilibrium in erect position. We demonstrated here for the first time that a build-up of equilibrium disturbances occurs at the first stage of hypokinesia, whereas from the 30th day on there is relative stabilization of stabilogram parameters and further extension of hypokinesia does not lead to drastic worsening of stability in vertical position. What we have described above is of great practical importance to elaboration of measures for the prevention of postural disturbances in cosmonauts. Establishment of the fact that the role of vision in maintaining equilibrium in erect position increases in the second half of the hypokinetic period is of practical importance.

According to the results of the functional tests, functional changes in the vestibular system--deconditioning thereof--is one of the causes of impaired equilibrium due to hypokinesia. The disturbances referable to postural equilibrium that occur after space flights are probably also attributable, to some extent, to functional changes in the vestibular analyzer, which is one of the important elements of the complex system of postural regulation in man. This circumstance must be taken into consideration in refining the set of preventive measures.

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PROGNOSTIC VALUE OF BLOOD CHOLESTEROL LEVEL IN HEALTHY SUBJECTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 13 Nov 80) pp 30-33

[Article by V. V. Vlasov]

[English abstract from source] The paper describes a new approach to the formation of "normal" (reference) values: the reference group is to be formed from subjects in good health condition at the time of the first and repeated (say, five years later) examinations; the reference group cannot include people developing chronic diseases within this time interval.

[Text] The hypothesis of the norm [normal] as the most common variant of organisms is a reflection of the principle of optimality of living organisms [1]. In particular, the hypothesis was expounded that "normal" values (reference values for healthy individuals [2]) can be statistically formed by screening a random group of people or even as a characteristic of a certain heterogeneous random clinical group (reference group [3]). However, it is apparent that the most widespread tag [sign] is not necessarily the best for an individual organism and population as a whole. For this reason, the prevalent view is that the "norm" is a statistical characteristic of only healthy people. In practice, such a conception is more expedient, since it yields more homogeneous data and permits formation of a narrower reference interval and, consequently, better differentiation between healthy and sick organisms [4, 5]. An important problem in forming "norms" is the similarity [unity] of requirements with regard to the health status of individuals making up the reference group [4]. As we know, there are no generally accepted health criteria. For this reason, data obtained on individuals who are the most "free of diseases," undergoing strict medical screening and under constant medical supervision, are of particular interest.

At the present time, it is generally recognized that the transition from a state of good health to a state of disease is extended in time. At the same time, it is often assumed that the characteristics of this "third state" (premorbid) occupies an intermediate place between the range of characteristics of healthy and sick individuals. There are no exhaustive grounds for this assumption, since the process of development of a disease may be nonlinear.

Apparently, individuals in a premorbid state, like those who are sick, should not be included in the reference group of healthy subjects. The main difficulty of

applying this thesis is attributable to the fact that methods have not been developed for diagnosing premorbid states. Such states should be characterized by an increased risk of development of a disease in a clinical form. Conversely, the probability of development of chronic diseases diagnosed by conventional methods should be lower among healthy individuals. On the basis of the foregoing, it may be assumed that the reference group used to form "norms" must consist of subjects in good health, who are capable of retaining good health for a specific, rather long period of time.

Methods

We studied the records of in-hospital examination of 335 pilots and navigators at the age of 34-36 and 39-41 years (second time). We selected blood plasma cholesterol level, assayed by the method of Il'k, as the analyzed parameter. In our survey of morbidity, we did not take into consideration the sequelae of trauma, refraction anomalies or certain surgical diseases (varicocele, Dupuytren's contracture and others).

Results and Discussion

It was established that blood serum cholesterol concentration in healthy flight personnel 35 years of age differs from the recommended reference range and constitutes 5.78±0.73 mM/ℓ (M±σ; Figure 1, [6]). Relative hypercholesterolemia had been demonstrated in flight personnel previously, and it was evaluated as an adverse phenomenon, as a high risk factor for development of atherosclerosis [7-9]. Indeed, cardiovascular pathology is in first place among reasons for disqualifying flight personnel for health reasons and among causes of death [10, 11]. At the same time, it was determined that life expectancy of individuals in the flying profession is above the average for the general population [10], while diseases of the cardiovascular system occur less often among pilots and are less often the cause of death than in the other population [10, 12]. Consequently, the blood cholesterol level in excess of the conventional "norm" among flight personnel cannot be given such an unequivocal evaluation.

Flight personnel constitute a large group of individuals who undergo medical screening prior to professional training. For this reason, we cannot rule out the fact that "universal norms" are not fully applicable to evaluate the health status of pilots. A special norm could be obtained by a traditional method, by examining healthy flight personnel. However, within this group, we could single out a more homogeneous group of people who retain their good health for a specific period of time until they are re-examined. The characteristics of individuals with a low risk of developing diseases, who make up this reference group, can apparently be taken as the norm with the most justification.

The blood cholesterol concentration was higher in subjects who retained good health up to the age of 40 years than in healthy subjects tested at 35 years of age (5.93±0.72 mM/ℓ; $P<0.01$), and it was higher than among those who contracted chronic diseases during this period, with the exception of diseases of the spine (5.36±0.6 mM/ℓ; $P<0.01$). Thus, chronic diseases developed more often among individuals with relative low, "normal" blood cholesterol level in the traditional interpretation ($P<0.001$). Using the formula of Bayes, we can calculate the probability of retaining good health among individuals 35 years of age (see Figure 1), as a function of blood cholesterol concentration. As we see, the probability of

retaining good health (Q_1, Q_2) increases in the presence of relative hypercholesterolemia. This function is particularly marked in the first 1-4 years after the first examination. Consequently, the above method can be used to form norms that are of both diagnostic and prognostic value. Within the period of such a norm, the probability of retaining good health changes, and this enables us (for example, for purposes of vocational screening) to narrow down the interval in accordance with the specified probability of retaining good health.

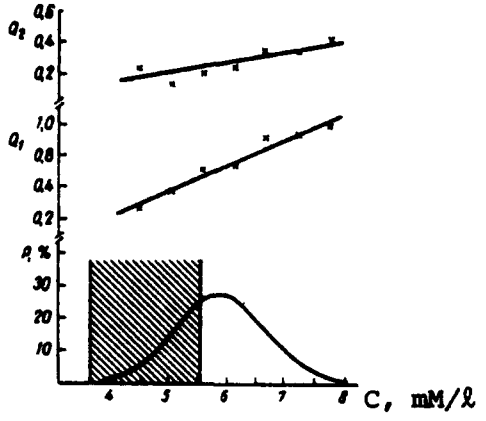

Figure 1.
Some parameters characterizing 35-year old flight personnel according to blood serum cholesterol concentration. Overall probability that good health will be retained by healthy people up to the age of 39 years is taken as 0.75 and at 40 years as 0.25. Cross-hatched area illustrates the range of the "traditional" norm

P) distribution of individuals
Q_1) probability of retaining health to 39 years of age
Q_2) same to 40 years of age

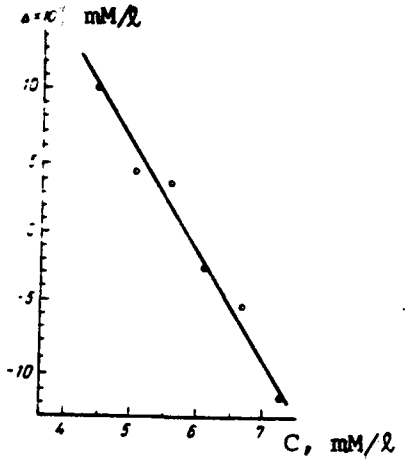

Figure 2.
Changes in blood serum cholesterol concentration (C, mM/ℓ) in 40-year old individuals as a function of level thereof at the age of 35 years
Δ) mean change in concentration over 5-year period (mM/ℓ)

These patterns are largely valid for individuals suffering from some chronic disease at the age of 35 years. In this group of people, hypocholesterolemia is associated with a higher probability of being disqualified for health reasons before the age of 45 years. In the case of relative hypocholesterolemia (less than 4.68 mM/ℓ), there is 1.72 times greater probability ($P<0.01$) of diseases of the gastrointestinal tract, nervous and cardiovascular systems determining morbidity of the population as a whole and flight personnel in particular. The probability of development of organic myocardial pathology is greater. At the same time, the incidence of diseases of the spine is 3.56 times higher with a cholesterol concentration of 5.72-6.76 mM/ℓ ($P<0.001$). Consequently, the changes that develop in the premorbid period have some specific features.

The changes in cholesterol concentration over a 5-year period depend on concentration thereof at the age of 35 years. In subjects who presented relative hypercholesterolemia at 35 years of age, not only was there no increase in blood cholesterol level, it even declined at 40 years. The increase in concentration of cholesterol was most marked in subjects with relative hypocholesterolemia, which conforms with the law of the base value [13] (Figure 2). Thus, in 35-year-old subjects with relative hypocholesterolemia, there was an increase in probability of development of hypercholesterolemia at the age of 40 years and higher risk of chronic diseases.

In other words, the premorbid state is demonstrable 1-5 years prior to development of disease in a clinical form, and it is characterized, in particular, by a decrease in cholesterol concentration of blood serum. Maximum intensity of hypocholesterolemia is observed 1-3 years before the disease is diagnosed by conventional methods. According to the literature, hypocholesterolemia preceding an increase in blood cholesterol is also demonstrable in model experiments [14, 15].

At the age of 40 years, in the presence of relative hypercholesterolemia (6.24 mM/ℓ or more), the share of organic myocardial diseases increases by 2.1 times among causes of disqualification for health reasons up to the age of 45 years ($P<0.05$). In the group of subjects suffering from chronic disease at the age of 40 years, the probability of being disqualified before the age of 45 years in the presence of relative hypercholesterolemia (5.72 mM/ℓ or more) was 1.68 times higher ($P<0.01$). Thus, there are age-related distinctions to the link between risk of worsening of health status in general and development of myocardial disease in particular, on the one hand, and the value of a specific parameter of the body (blood serum cholesterol concentration). It can be assumed that changes develop at the preclinical stage of a disease, which are related to a number of factors, in particular, age and prior diseases.

For analysis of the mechanisms of development of a premorbid state it is not enough to merely test cholesterol level in blood serum. Evidently, a study conducted on the basis of records of a single hospital does not enable us to recommend unconditionally the use of the reference interval we obtained for cholesterol. At the same time, we can formulate the following main conclusions within the context of the purpose of our study, i.e., the question of methods of forming "norms."

It is desirable to form reference values for healthy people as a statistical characteristic of organisms capable of retaining good health over a long period of time. In the older age groups, where formation of a reference group of healthy subjects is more problematic, time of retention of professional fitness or life expectancy could serve as a criterion for screening a reference group of a specific age. Deviation from the reference intervals formed in this manner indicates not only an increase in probability of presence of a disease, as is the case with the use of traditional "norms," but is associated with a higher probability of development of disease in the immediate future, which enables us to forecast the health status and implement preventive measures. The interval can be narrowed in accordance with a specified probability of preserving good health for the purpose of vocational screening.

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EFFECT OF EXERCISE ON REACTIONS TO BREATHING A GAS MIXTURE WITH 5% CARBON DIOXIDE AND 14% OXYGEN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 13 Dec 80) pp 33-35

[Article by N. P. Krasnikov]

[English abstract from source] The effect of a hypoxic-hypercapnic gas mixture (5% CO_2 + 14% O_2) on the exercising man was studied. At a low work load inhalation of this gas mixture inhibited gas exchange, and after 10 month training stimulated it. Thus, increase in physical endurance was followed by increase in human resistance to O_2 deficiency and CO_2 excess in the breathing mixture.

[Text] There are conflicting opinions concerning the effect of hypercapnia on exchange of gases. Some authors maintain that carbon dioxide inhibits gas exchange [1-3] and others, that it has a stimulating effect [4-7]. There is very little information in the literature concerning the effect of calisthenics on endurance of hypoxic-hypercapnic gas mixtures.

Our objective here was to examine the distinctions of gas exchange and external respiration in individuals differing in degree of physical conditioning breathing a hypoxic gas mixture with high concentration of carbon dioxide, and to determine whether it is possible to enhance general resistance to a shortage of oxygen and excess carbon dioxide in inhaled air as endurance builds up.

Methods

A total of 22 healthy men 18-23 years of age, who were divided into 2 groups, participated in our studies. The main group consisted of 12 men who exercised regularly on a bicycle track to increase general and special endurance, and the control group consisted of 10 men who did not specially exercise. The tests with hypoxic-hypercapnic gas mixtures were conducted at the start of the studies (base data) and after long-term physical conditioning. We examined the following parameters: heart rate (HR), respiration rate (RR), pulmonary ventilation, tidal volume, oxygen uptake, carbon dioxide output, volume of physiological "dead" space, alveolar ventilation, ventilation equivalent, respiratory quotient, coefficient of utilization of oxygen, oxygen pulse, oxygen content of alveolar and exhaled air. These parameters were recorded in the 10th min of breathing normoxic (20.9% O_2), hypoxic (14.0% O_2) and hypoxic-hypercapnic (5.0% CO_2 + 14.0% O_2) gas mixtures. The tests were conducted in the morning, after waking up, in a state of relative

rest. Gas exchange was examined in an open system. The gas mixture with a specified concentration passed from a tank into a KP-24 oxygen instrument, then through a valve box and mouthpiece into the subject's lungs (during inspiration). Exhaled air was collected in Douglas bags. We used the Soviet GVV-2-10 instrument to analyze gas samples. The calculation of volumetric parameters of oxygen uptake and carbon dioxide output was made by the method of Douglas-Haldane. HR was recorded on an ELKAR-6 electrocardiograph. Maximum physical work capacity was determined during work on a VE-02 bicycle ergometer by the method of stepped increase in load up to total fatigue and refusal to pedal [8].

Results and Discussion

Base data were recorded while breathing with the use of specified gas mixtures before conditioning exercise with relatively low physical work capacity (322.0±9.9 kg-m/kg body weight). Inhalation of hypoxic mixture failed to demonstrate a basic difference in HR and pulmonary ventilation parameters, as compared to levels recorded when breathing with air (20.9% O_2). However, the gas-exchange parameters presented appreciable differences (see Table). Thus, oxygen content of alveolar and exhaled air diminished by 42.5% ($P<0.001$) and 36.6% ($P<0.001$) when using a hypoxic breathing mixture, and oxygen uptake decreased by 14.4% ($P<0.02$). As a result of these changes, there was a 10.0% increase ($P<0.02$) in respiratory quotient, while oxygen pulse decreased by 23.6% ($P<0.02$). These dynamics were indicative of poorer oxygen supply to the body [7]. Analogous changes were also observed in the control group.

Use of the hypoxic-hypercapnic breathing mixture was associated with more profound functional changes. Mean respiratory volume and pulmonary ventilation increased reliably ($P<0.001$), while RR did not change. Nevertheless, the efficiency of pulmonary ventilation diminished substantially, as confirmed by the increase ($P<0.001$) in ventilation equivalent and volume of physiological dead space. The hypoxic-hypercapnic gas mixture also elicited a rather significant ($P<0.001$) decrease in oxygen uptake. There was a more than 8-fold decrease in output of carbon dioxide with a constant concentration of inhaled "exogenous" carbon dioxide, as compared to the level recorded with the use of air for breathing. In some cases, we observed "absorption" of carbon dioxide, while oxygen uptake diminished to 60 mℓ/min. The concentration of oxygen in samples of alveolar and exhaled air decreased by 33.0% ($P<0.001$) and 24.0% ($P<0.001$), respectively, as it did when using the hypoxic breathing mixture. In the opinion of some authors, excessive carbon dioxide is formed in tissues when using a hypoxic-hypercapnic gas mixture, which inhibits metabolism and, consequently diminishes oxygen uptake [6, 7].

As we have already indicated, the subjects were re-examined with the use of the above-mentioned gas mixtures after 10 months of regular exercise. The HR and pulmonary ventilation did not change (see Table). There was a 67.3% increase ($P<0.001$) in oxygen uptake with use of the hypoxic-hypercapnic breathing mixture, as compared to base data, carbon dioxide output increased by 215.0% ($P<0.02$), and there was reliable ($P<0.001$) increase in parameters of oxygen pulse and coefficient of oxygen utilization. There was a decrease ($P<0.05$) of ventilation equivalent and volume of physiological dead space, with concurrent increase in alveolar ventilation ($P<0.01$). This was associated with 18.0±3.1% (380.0±12.0 kg-m/kg body weight, $P<0.01$) increase in physical work capacity. As physical endurance increased, there was a decrease in oxygen content of exhaled air, while oxygen utilization increased by 0.5% ($P<0.02$) with the hypoxic load and by 0.7% ($P<0.001$)

with the hypoxic-hypocapnic one. These changes were indicative of more effective oxygen supply in the main group of subjects [5, 6]. No reliable changes were demonstrated in the control group.

Dynamics of parameters of external respiration and gas exchange after a period of physical training with use of hypoxic and hypoxic-hypercapnic gas breathing mixtures (M±m). Initial parameters when breathing air (20.9% O_2) are given in parentheses

Parameter	14 % O_2		5 % CO_2 + 14 % O_2	
	base data	after 10 mos. conditioning	base data	after 10 mos. conditioning
HR, per min	60,0±2,9 (54,0±2,4)	60,0±2,8	55,0±2,4	55.0±2,2
RR, per min	17,0±2,2 (16,0±2,2)	13,0±1,7	16,0±1.7	14,0±1,6
$\dot{V}_E$, ℓ/min	11,7±0,6 (12,8±0,9)	11,6±0,6	22,2±1,3	24,9±1,6
$\dot{V}_T$, mℓ	653,0±61,0 (787,0±82,6)	873,0±90,0	1455,0±100,0	1772,0±142,0
$\dot{V}O_2$, mℓ/min	290,0±10,7 (339,0±12,3)	326,0±12,0	171,0±12,0	287,4±13,9
$\dot{V}CO_2$, mℓ/min	298,0±13,9 (325,0±17,8)	307,8±17,7	39,0±11,0	84,2±12,6
$\dot{V}_D$, ℓ/min	4,66±0,38 (4,26±0,78)	3,83±0,75	15,39±1,67	11,0±0,9
$\dot{V}_A$, ℓ/min	5,63±0,38 (7,03±0,64)	6,57±0,55	7,54±0,64	13,5±1,5
VE,	0,42±0,02 (0,37±0,02)	0,37±0,01	1,7±0,36	0,9±0,06
R	1,03±0,02 (0,93±0,02)	0,95±0,03	0,31±0,07	0,3±0,05
CUO_2, mℓ/min	28,6±1,7 (32,5±1,7)	33,7±0,9	8,1±0,6	13,0±1,01
OP, mℓ/beat	4,86±0,35 (6,36±0,44)	5,40±0,31	3,08±0,28	5,5±0,34
C_AO_2, vol.%	8,8±0,32 (15,3±0,32)	9,0±0,35	11,9±0,19	11,6±0,23
C_EO_2, vol.%	11,1±0,14 (17,5±17)	10,6±0,11	13,3±0,09	12,6±0,13

Key:
- $\dot{V}_E$) pulmonary ventilation
- V_T) tidal volume
- $\dot{V}O_2$) oxygen uptake
- $\dot{V}CO_2$) carbon dioxide output
- V_D) physiological dead space volume
- $\dot{V}_A$) alveolar ventilation
- VE) ventilation equivalent
- CUO_2) coefficient of oxygen utilization
- R) respiratory quotient
- OP) oxygen pulse
- C_AO_2) oxygen content of alveolar air
- C_EO_2) oxygen content of exhaled air

It is known that acclimatization to high altitudes and conditioning in pressure chambers enhance body resistance to a number of extreme factors, including heavy exercise [9, 10]. Regular calisthenics enhance resistance to hypoxic and hypoxic-hypercapnic gas mixtures, as shown by our study. For this reason, we are justified in concluding that a high level of physical conditioning can serve as one of the means of expanding the functional capacities of the body for the purpose of improving endurance of diverse extreme factors.

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SENSITIVITY TO ANTIBIOTICS OF LACTOBACILLI FROM DIGESTIVE TRACT OF SOYUZ-13 AND SALYUT-4 CREW MEMBERS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 8 Dec 80) pp 36-39

[Article by A. A. Lentsner, M. E. Tyuri, Kh. P. Lentsner, M. E. Mikel'saar, V. M. Shilov, N. N. Liz'ko and G. D. Syrykh]

[English abstract from source] Sensitivity to 10 antibiotics of 411 lactobacillar strains isolated from the saliva and feces of crewmembers who made 8-, 30- and 63-day flights was determined. Antibiotic sensitivity remained unchanged even in the 63-day flight. The antibiotics tested produced different effects on the lactoflora that varied from gentle--polymyxin and gentamycin, less gentle--neomycin and monomycin, to hazardous--penicillin and erythromycin, then rifampicin and levomycetin, and, finally, tetracyclin and oleandomycin.

[Text] The probability of diseases related to attenuation of nonspecific constitutional resistance and changes in the microflora of cosmonauts increases with increase in duration of space flights, so that antibiotics must be stowed in the onboard medicine chest [1]. In turn, the use of antibiotics could lead to development of dysbacteriosis [2, 3], in particular, decrease in number of lactobacilli in the intestinal microflora [4, 5]. Consequently, when stocking assortments of drugs for cosmonauts, one must take into consideration the sensitivity of lactobacilli to antibiotics and make provisions for speedy restoration of lactoflora of the digestive tract. At the same time, there is very little information about the sensitivity of different species of lactobacilli to different antibiotics, and no studies at all of the effects of space flight conditions on antibiotic resistance of lactobacilli in the human digestive tract.

We submit here the results of a study of antibiotic sensitivity of lactobacilli isolated from saliva and feces of five cosmonauts, who participated in an 8-day flight aboard Soyuz-13 spacecraft, as well as 30- and 63-day flights aboard the Salyut-4 orbital station, before and after these flights.

Methods

We studied a total of 411 strains: 112 from saliva and 299 from feces. They consisted of 6 species: Lactobacillus acidophilus (58), L. salivarius (94), L. casei

(137) (supspecies casei 70, subsp. rhamnosus 54, subsp. alactosus 13), L. plantarum (19), L. fermentum (62) and L. brevis (41).*

Table 1. Characteristics of paper disks

Product	Manufacturer	Concentr. µg/disk	Product	Manufacturer	Concentr. µg/disk
Ampicillin	Lachema Co.	20	Spiramycin	Lachema Co.	20
Vancomycin	"	50	Streptomycin	USSR	30
Penicillin	USSR	10	Tetracycline	"	30
Ristomycin	"	30	Chloramphenicol (levomycetin)	"	30
Cephaloridine	Lachema Co.	10			
Gentamicin	"	20	Erythromycin	"	15
Lincomycin	"	10	Novobiocin	"	15
Monomycin	USSR	30	Rifampicin	Lachema Co.	10
Neomycin	"	30	Polymyxin	USSR	300
Oleandomycin	"	15	Furadantin	Lachema Co.	100

Table 2.
Evaluation of results

Diameter of retarded growth zone, mm	Sensitivity	Score
Less than 10	Resistant	0
10-20	Moderately resistant	1
21-30	Moderately sensitive	2
Over 30	Sensitive	3

We tested lactobacillus sensitivity to 19 products (Table 1). We used the method of diffusion in agar with paper disks [6]. We worked with domestically manufactured and Lachema Co. (CSSR) paper disks containing various standard concentrations of the products (see Table 1). MRS-1, MRS-2 and MRS-5 nutrient media were used [7, 8].

Sensitivity of a strain to each antibiotic was evaluated according to diameter of retarded growth zone around the corresponding disk (Table 2).

Results and Discussion

Table 3 lists summary data on sensitivity of the tested strains to antibiotics. They indicate that the sensitivity of lactobacilli to different antibiotics is not the same. Moreover, we demonstrated certain interspecific differences. Sensitivity of the strains was unrelated to either the biovar of lactobacilli or subspecies of L. casei. For this reason, the results of our studies are discussed only according to species and exactly as submitted in Table 3.

Lactobacilli were the most sensitive to penicillin and erythromycin, then rifampicin and levomycetin, being the most resistant to polymyxin and gentamicin, then neomycin and monomycin. For example, none of the 411 tested strains was resistant to penicillin or erythromycin, but all were resistant to polymyxin. Most strains were moderately sensitive to rifampicin and levomycetin; however they were moderately resistant or resistant to neomycin and monomycin.

*Lactobacilli were identified in the course of studies of lactoflora of cosmonauts.

Table 3. Incidence of strains differing in sensitivity to antibioltics according to species (%)

Lactobacillus species	Sensitivity, score	Ampicillin	Vancomycin	Penicillin	Ristomycin	Cephaloridine	Gentamicin	Lincomycin	Monomycin	Neomycin	Oleandomycin	Spiramycin	Streptomycin	Tetracycline	Chloramphenicol	Erythromycin	Novobiocin	Rifampicin	Furadantin
L. acidophilus (58 strains)	0	0,0	1,8	0,0	0,0	0,0	50,0	1,7	29,3	36,2	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	1,8
	1	25,9	22,4	1,7	65,5	0,0	50,0	27,6	44,8	55,2	0,0	15,5	31,0	1,7	3,5	0,0	3,4	3,5	32,6
	2	58,6	62,1	5,2	29,3	56,9	0,0	20,7	25,9	8,6	44,8	65,5	53,5	39,7	19,0	6,9	60,4	41,4	55,2
	3	15,5	13,7	93,1	5,2	43,1	0,0	50,0	0,0	0,0	55,2	19,0	15,5	58,6	77,5	93,1	36,2	55,1	10,4
L. salivarius (94 str.)	0	8,5	100,0	0,0	100,0	0,0	23,4	0,0	3,2	6,4	0,0	0,0	2,1	0,0	0,0	0,0	0,0	0,0	0,0
	1	54,2	0,0	0,0	0,0	35,1	76,6	1,1	75,5	85,1	1,1	19,1	51,1	0,0	0,0	0,0	2,1	0,0	3,2
	2	36,2	0,0	8,5	0,0	61,7	0,0	41,5	19,2	8,5	74,5	70,2	44,7	36,2	50,0	14,9	31,9	32,0	80,9
	3	1,1	0,0	91,5	0,0	3,2	0,0	57,4	2,1	0,0	24,4	10,7	2,1	63,8	50,0	85,1	66,0	68,0	15,9
L. casei (137 str.)	0	16,8	100,0	0,0	100,0	0,0	64,2	0,0	20,4	24,1	0,0	0,0	5,9	0,0	0,0	0,0	0,0	0,0	11,7
	1	73,0	0,0	1,5	0,0	81,8	35,8	27,0	79,6	75,9	14,6	82,5	93,4	6,6	1,5	0,0	5,1	2,2	82,5
	2	10,2	0,0	67,9	0,0	18,2	0,0	61,3	0,0	0,0	84,7	17,5	0,7	67,2	77,4	73,7	84,7	61,3	5,8
	3	0,0	0,0	30,6	0,0	0,0	0,0	11,7	0,0	0,0	0,7	0,0	0,0	26,2	21,1	26,3	10,2	36,5	0,0
L. plantarum (19 str.)	0	0,0	100,0	0,0	100,0	0,0	52,6	0,0	21,1	15,8	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
	1	32,0	0,0	10,0	0,0	84,2	47,4	5,2	78,9	84,2	42,1	94,7	94,7	0,0	0,0	10,5	10,5	10,5	52,6
	2	68,0	0,0	53,0	0,0	15,8	0,0	47,4	0,0	0,0	57,9	5,3	5,3	57,9	89,5	84,2	84,2	89,5	47,4
	3	0,0	0,0	37,0	0,0	0,0	0,0	47,4	0,0	0,0	0,0	0,0	0,0	42,1	10,5	5,3	5,3	0,0	0,0
L. fermentum (62 str.)	0	3,2	100,0	0,0	100,0	0,0	19,4	0,0	1,6	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
	1	12,9	0,0	0,0	0,0	14,5	76,9	8,1	79,0	87,1	11,3	33,9	71,0	4,8	0,0	0,0	27,4	0,0	8,1
	2	67,7	0,0	8,1	0,0	50,0	9,7	19,4	19,4	11,3	79,0	50,0	14,5	69,4	27,4	46,8	53,2	24,2	54,8
	3	16,2	0,0	91,9	0,0	35,5	0,0	72,5	0,0	1,6	9,7	16,1	14,5	25,8	72,6	53,2	19,4	75,8	37,1
L. brevis (41 str.)	0	7,3	100,0	0,0	100,0	0,0	7,3	4,9	2,4	4,9	0,0	0,0	4,9	0,0	0,0	0,0	0,0	0,0	0,0
	1	70,7	0,0	2,4	0,0	51,2	90,3	26,8	92,8	92,7	7,3	24,4	73,2	12,2	0,0	0,0	31,7	0,0	29,3
	2	22,0	0,0	29,3	0,0	48,8	2,4	43,9	2,4	0,0	85,4	73,2	19,2	61,0	58,5	29,3	29,3	34,1	63,4
	3	0,0	0,0	68,3	0,0	0,0	0,0	24,4	2,4	2,4	7,3	2,4	2,4	26,8	41,5	70,7	39,0	65,9	7,3

Note: All strains were resistant to polymyxin.

We demonstrated the selective effect of vancomycin and ristomycin L. acidophilus. All strains of the other lactobacillus species were resistant to these antibiotics, but none were found among L. acidophilus strains.

Table 4.
Antibiotic sensitivity of lactobacilli

Species	Number of sensitive strains	
	at least 1	at least 10%
L. acidophilus	15	14
L. salivarius	14	10
L. casei	8	7
L. plantarum	5	3
L. fermentum	14	12
L. brevis	13	7

Note: We listed strains with a retarded growth zone of over 30 mm.

The attitude of a microbe toward antibiotics can be evaluated by the number of preparations with sensitive strains. According to this parameter, L. acidophilus, L. salivarius, L. fermentum and L. brevis were much more sensitivie to antibiotics than L. casei and, particularly, L. plantarum (Table 4). Yet L. acidophilus, L. fermentum and L. salivarius are the most common resident microflora of man, while L. plantarum is the most scarce [9-11].

It should be noted that the sensitivity of the tested strains to antibiotics was unrelated to the cosmonaut from which they were isolated, or to whether they were isolated from saliva or feces, before or after a flight. Thus, the conditions of even the 63-day flight aboard Salyut-4 orbital station did not elicit changes in sensitivity of lactobacilli of the human digestive tract to antibiotics. True, the cosmonauts did not take any antibiotics in the course of this flight [1].

The obtained data lead us to expect that polymyxin and gentamicin are the most sparing products for lactoflora. Polymyxin affects only Gram-negative bacteria, while gentamicin affects Pseudomonas aeruginosa, E. coli, microorganisms of the genera Proteus, Salmonella, Shigella, Staphylococcus and others [12]. Neomycin and monomycin, which have a broad spectrum of action, are relatively sparing [12, 13].

From the standpoint of lactoflora, penicillin and erythromycin are particularly dangerous, followed by rifampicin and levomycetin and, finally, tetracycline and oleandomycin. It should be noted that, in experiments on white mice, levomycetin and tetracycline caused drastic decrease in quantity of lactobacilli in feces of experimental animals [4]. Penicillin [14], erythromycin combined with streptomycin and nystatin [5] had an analogous effect.

Lactobacterin should be included in the onboard medicine chest, and it should be prescribed for intake during and after antibiotic therapy in order to correct the undesirable changes in microflora of the digestive tract as a result of antibiotic intake. Strain L. fermentum 90T-S4, which is used for production of lactobacterin, contains no plasmid DNA, so that the product can be used on a wide scale without danger of spreading antibiotic resistance [15].

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STUDY OF DIGESTIVE TRACT MICROFLORA OF SOYUZ-13 AND SALYUT-4 CREWS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 8 Dec 80) pp 39-43

[Article by A. A. Lentsner, Kh. P. Lentsner, M. E. Mikel'saar, V. M. Shilov, N. N. Liz'ko, G. D. Syrykh and V. I. Legen'kov]

[English abstract from source] The species composition and biology of lactoflora of the saliva and feces of crewmembers from 8-, 30- and 63-day flights was investigated. Altogether 593 strains of lactobacilli were examined. The space flights did not cause significant changes in physiology, biochemistry, antagonistic properties or lysozyme activity of lactobacilli. They did not change drastically or unify the species composition of the digestive lactoflora. However, transfer of lactobacilli from one crewmember to another cannot be excluded, its probability increasing with flight time.

[Text] It was previously shown that a year-old medical-technical study did not elicit significant change in species composition of fecal lactobacilli among the three participants thereof; however, it led to a decrease in quantity of lactobacilli in excreta [1]. There is no information in the literature about what happens to the digestive tract lactoflora in the course of space flights. Yet lactobacilli, which are indigenous, resident microorganisms, are closely associated with epithelial cells of the mucosa, and they play a substantial role in implementing the protective function of the microflora [2-4], in particular, with regard to pathogenic viruses [5]. Moreover, there are individual distinctions to this flora in healthy people [1, 3, 6]. Consequently, it is imperative to make a thorough and comprehensive study of both the lactoflora of cosmonauts and biology of microorganisms that make it up.

Our objective here was to study the species composition of lactoflora of saliva and feces in members of three crews, before and after space flights: participants of the 8-day flight aboard Soyuz-13 spacecraft, as well as the crews involved in 30- and 63-day flights aboard the Salyut-4 orbital station. We also examined antagonistic properties and lysozyme activity of isolated lactobacilli. For a long time, the protective function of lactobacilli has been related by researchers to their antagonistic properties in relation to other microorganisms. Lysozyme is involved in imparting constitutional resistance [7], and it has a stabilizing effect on the microflora [8]. It was recently established that some lactobacilli are capable of producing lysozyme [9].

Methods

In all, we studied 593 strains of lactobacilli, 199 from saliva and 394 from feces

We used a modified cat-tail ["rogoz"?] acetate agar and MRS-4 nutrient medium containing sorbic acid to isolate lactobacilli. The lactobacilli were identified by their physiological and biochemical properties, with the use of 16 tests.

The antagonistic properties were tested against Escherichia coli, Shigella newcastle, Staphylococcus aureus and Streptococcus faecalis. We calculated the indicators of antagonistic activity of species, subspecies and biovars of lactobacilli in order to compare antagonistic properties of different forms thereof. For this purpose, we first added the scores reflecting the degree of antagonistic activity of each strain against the different test microorganisms, then the obtained figures were added according to taxons and the obtained sums were divided by the number of corresponding strains. With such calculations, the maximum value of the parameter of antagonistic activity does not exceed 12.

Lysozyme activity was demonstrated by the method of agar plates on solid nutrient medium containing an autoclaved suspension of micrococcus.

The techniques for isolating and testing lactobacilli were described previously [3, 9, 10].

Results and Discussion

The strains studied were referable to seven species of lactobacilli, there being three subspecies--subsp. casei, subsp. rhamnosus and subsp. alactosus--among the strains of Lactobacillus casei (Table 1). L. salivarius was represented by the largest number of strains (174) and L. cellobiosus by the smallest (2). We encountered all of the biovars of these microorganisms that we differentiate [3] among the strains of L. acidophilus, L. salivarius, L. casei subsp. casei, L. plantarum, L. fermentum and L. brevis. There was prevalence of biovar I among L. plantarum, II among L. salivarius, L. casei subsp. casei and L. brevis, and biovar III among L. fermentum. It should be noted that we were unable to isolate a single strain of L. casei subsp. casei I, L. plantarum and L. cellobiosus from saliva, unlike feces. Thus, we isolated the same lactobacilli from the tested cosmonauts as are encountered the most frequently in the digestive tract of healthy people [1, 3, 6, 11].

Table 1. Species composition of the lactobacillus strains studied

Species & biovar	Numb. of strains		Species & biovar	Number of strains	
	saliva	feces		saliva	feces
L. acidophilus I	35	28	L. plantarum I	—	15
L. acidophilus II	46	7	L. plantarum II	—	4
L. salivarius I	8	41	L. fermentum I	5	4
L. salivarius II	25	100	L. fermentum II	6	7
L. casei			L. fermentum III	13	18
subsp. casei I	—	4	L. fermentum IV	13	6
subsp. casei II	5	67	L. brevis I	3	4
subsp. rhamnosus	2	61	L. brevis II	35	16
subsp. alactosus	3	10	L. cellobiosus	—	2

Summary data on the physiological and biochemical properties of the isolated lactobacilli are listed in Table 2. They are consistent with the relevant information in the literature pertaining to human lactobacillary microflora [1, 3, 11]

Table 2. Properties of lactobacillus strains studied

Character	L. acidophilus	L. salivarius	L. casei			L. plantarum	L. fermentum	L. brevis	L. cellobiosus
			subsp. casei	subsp. rhamnosus	subsp. alactosus				
	number of strains								
	116	174	76	63	13	19	72	58	2
Gas from glucose	–	–	–	–	–	–	+	+	–
Growth with 0.4% tipol*	–	–	–	–	–	+	–	±(7)	±(1)
Growth at 15°C	–	–	+	+	+	+	–	±(7)	–
Cellobiose	–	+	±(72)	±(62)	+	±(5)	–	–	–
Melezitose	±(106)	–	+	+	+	+	–	–	–
Maltose	–	±(105)	–	+	–	±(4)	–	–	–
Mannose	–	–	+	+	+	+	–	–	–
Salicin	+	+	+	+	+	–	–	±(57)	–
Volutin granules	+	+	+	±(62)	+	+	–	+	–
Acid in milk, %	+	+	+	±(60)	+	+	±(67)	+	–
	+	+	+	+	+	+	±(50)	–	–
	+	+	+	+	–	+	±(60)	±(56)	–
	±(111)	±(125)	+	+	+	+	–	±(51)	±(1)
	±(53)	+	+	+	+	+	±(32)	±(31)	±(1)
	±(5)	–	±(4)	±(1)	–	±(1)	±(32)	±(38)	–
	0.1—4.4	0.2—2.5	0.3—2.5	0.5—2.6	0.5—2.4	0.6—1.4	0.1—1.9	0.1—2.1	0.9—1.3
Antagonistic activity	2.3	6.7	7.3	7.2	7.9	5.1	4.2	5.3	7.0
Lysozyme activity	–	–	–	–	–	–	±(69)	–	–

*A laundry aid.

Note: Number of strains reacting positively is given in parentheses.

A total of 496 strains (83.6%) presented antagonistic activity. The indicator of antagonistic activity was lowest in L. acidophilus--only 2.3 (see Table 2). It was about twice as high in L. plantarum, L. fermentum and L. brevis, and even 3 times higher in L. salivarius and L. casei. We failed to demonstrate any particular differences between biovars with regard to antagonistic activity. In this respect, the only exceptions were L. fermentum biovars: the indicator was 2.4 for biovar II, 3.5 for IV, 3.6 for I and even 5.5 for biovar III. Antagonistic activity of lactobacilli was unrelated to the energy of acid production. All of the strains of L. acidophilus, L. salivarius, L. casei, L. plantarum, L. brevis and L. cellobiosus were lysozyme-negative. On the other hand, 95.8% of the L. fermentum strains (69 out of 72) produced lysozyme.

Thus, antagonist strains were widely represented in the lactoflora of the subjects' digestive tract. The antimicrobial properties of L. acidophilus were inferior to those of other species, while lysozyme activity was inherent only in L. fermentum. The obtained findings are not in contradiction to what was expected, according to data in the literature [3, 9].

It should be specially stressed that the physiological, biochemical and antagonistic properties, as well as lysozyme activity, of the studied strains were unrelated to the material from which they were isolated. Consequently, even the conditions prevailing in the 63-day flight aboard Salyut-4 orbital station did not elicit profound changes in biology of lactobacilli in the digestive tract of its participants, at least not with regard to the characters we studied. On the other hand,

studies pursued in pressure chambers and spacecraft mockups revealed changes in biology of such representatives of human microflora as Staphylococcus aureus, Escherichia coli and Clostridium perfringens [12, 13]. For example, a decrease in antagonistic activity of E. coli was reported [12].

Table 3. Species composition of lactoflora of cosmonauts' saliva and feces before and after flights

Cosmonaut	Saliva		Feces	
	preflight	postflight	preflight	postflight
	8-day flight aboard Soyuz-13 spacecraft			
CDR*	aI fII fIII brII (4)	aI aII sI sII fI fII fIII fIV brI brII (10)	aI sI sII brII (4)	aI sI sII (3)
FLE	aI aII sII brII (4)	ca (1)	aI aII sI sII ccI ccII cr brII (8)	sII ccII cr brII (5)
	30-day flight aboard Salyut-4 orbital station			
CDR	aII cr brII (3)	aII ccII cr (3)	aI ccII cr pI fIII brI (6)	ccII cr pI pII fIII (5)
FLE	aI aII sI ccII fIII brII (6)	aI aII sI fIII brII (5)	aI aII sI (3)	aI sI ccII cr pII fIII brII c (8)
	62-day flight aboard Salyut-4 orbital station			
CDR*	aI aII sII fII fIV (5)	aI aII sII fI fII fIII fIV (7)	aI aII sII ccII fI fIII fIV (7)	aI aII sI sII fII fIII (6)
FLE	none isolated	aI aII fII brII (4)	ccI ccII cr ca brI brII (6)	aI fI fII fIII fIV brI brII (7)

*Cosmonaut who participated in 8- and 63-day flights.

Note: Quantity of lactobacilli is given in parentheses.

Key:

aI, aII) L. acidophilus I and II
sI, sII) L. salvarius I and II
ccI, ccII) L. casei subsp. casei I and II
cr) L. casei subsp. rhamnosus
ca) L. casei subsp. alactosus
pI, pII) L. plantarum I and II
fI, fII, fIII, fIV) L. fermentum I, II, III and IV
brI, brII) L. brevis I and II
c) C. cellobiosus

Various lactobacilli (Table 3) were encountered in the digestive tract of all crew members of Soyuz-13 spacecraft and the two missions aboard Salyut-4 orbital station. We succeeded in demonstrating typical lactobacillary species in each participant, before and after the flights. A simpler species composition of lactoflora was observed only in the flight engineer (FLE) of Soyuz-13. There are data indicative of transfer of lactobacilli among crew members.

Eight-day flight aboard Soyuz-13 spacecraft: L. acidophilus I, L. fermentum II and III, and L. brevis II were demonstrated in saliva of the commander (CDR) before and after flight, while constant lactobacilli were not demonstrable in the saliva of the FLE; L. acidophilus I, L. salivarius I and II were encountered in feces of the CDR before and after flight; L. salivarius II, L. casei subsp. casei II and

L. casei subsp. rhamnosus were demonstrated in the FLE. We were unable to demonstrate exchange of lactobacilli between the cosmonauts.

Thirty-day flight aboard Salyut-4 orbital station: The constant lactobacilli found in the saliva of the CDR were L. acidophilus II and L. casei subsp. rhamnosus, with L. acidophilus I and II, L. salivarius I, L. fermentum III and L. brevis II consistently present in the FLE; in feces, L. casei subsp. casei II, L. casei subsp. rhamnosus, L. plantarum I and L. fermentum III were demonstrated in feces of the CDR before and after flight, and this applied to L. acidophilus I and L. salivarius I in the FLE. Evidently, L. casei subsp. rhamnosus had been transmitted into the digestive tract of the FLE, since this microorganism had been isolated before flight only from the CDR and after flight, in both cosmonauts.

Sixty-three-day flight aboard Salyut-4 orbital station: L. acidophilus I and II, L. salivarius II, L. fermentum II and IV were found before and after the flight in saliva of the CDR; no lactobacilli could be isolated before the flight from saliva of the FLE; lactoflora of the feces consisted of L. acidophilus I and II, L. salivarius II and L. fermentum III in the CDR before and after flight; only L. brevis I and II were present in the FLE. Evidently, there was transfer of L. acidophilus I, as well as L. fermentum biovars from the CDR to the FLE.

The results of examining the lactoflora of the cosmonaut who participated in the 8- and 63-day flights are of definite interest. As we know, the interval between these studies was about 1.5 years. In spite of this, we demonstrated in the saliva of this cosmonaut L. acidophilus I and L. fermentum II, and in feces L. acidophilus I and L. salivarius II before and after the 63-day flight, i.e., the same lactobacilli as were recorded as constant ones during the 8-day flight.

Thus, the conditions of the 8-, 30- and even 63-day flights did not lead to significant changes in species composition of digestive tract lactoflora or unification thereof in crew members. The results of studying the biology of isolated lactobacilli are also indicative of relative stability of lactoflora of the digestive tract.

The individual differences in lactoflora, its constancy and protective properties are related primarily to resident lactobacilli [1-4, 6]. Expressly the lactobacilli demonstrated both before and after flight can be interpreted as such forms. It is also interesting to note that among the resident lactobacilli in all cosmonauts there were some with distinct antagonistic activity (L. salivarius, L. casei, L. plantarum, L. fermentum III or L. brevis), whereas L. fermentum was the only lysozyme-positive species of these microorganisms in 4 out of 5 cosmonauts. All of the recent data in the literature are indicative of the rather important role of L. fermentum in resistance of the organism [14, 15] and regulation of enzymatic activity of the digestive tract [16]. This microorganism is also used in the production of lactobacterin [3, 9].

It is apparent from our findings that the thesis of reduction of species composition of microflora in a closed environment [17] does not apply to lactoflora. This is understandable, since simplification of species composition of digestive tract microflora can only occur due to microorganisms that are incapable of long-term self-support in the organism [17]. True, no drastic reduction of species composition of microorganisms was demonstrated in the microflora of the mouth and nose of astronauts of the Apollo spacecraft [18] or microflora of the integument and upper respiratory tract of participants in the joint flight of Apollo and Soyuz spacecraft

[19]. Nor were significant changes in species composition of fecal microflora demonstrated in the three participants of the test in a pressure chamber on the Skylab program [20].

In conclusion, it should be noted that we cannot rule out transfer of lactobacilli among crew members, and the probability thereof increases with increase in flight duration. This conforms with data in the literature concerning the relationship between microbial contamination of internal surfaces of the Salyut-4 orbital station and time spent there by people [21].

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EFFECTIVENESS OF DECOMPOSITION OF PLANT WASTE BY MICROORGANISMS UNDER AEROBIC CONDITIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 5 Jul 79) pp 44-45

[Article by I. L. Chernovich, L. M. Sidorova and N. A. Mal'tseva]

[English abstract from source] Degradation of plant wastes by means of microbial coenosis under aerobic conditions was studied. Efficiency of the process increased with increase in time and temperature. Microbial degradation of vegetable wastes was more complete than that of wheat wastes.

[Text] The waste from higher plants (straw, vegetable tops) must be converted into a form that can be assimilated by plants in closed life-support systems that are based on the cycle of matter.

Our objective here was to examine the effectiveness of microbiological mineralization of organic matter of wheat chaff and haulm of vegetable plants under aerobic conditions.

Methods

A microbial cenosis adapted for decomposition of plant cellulose was obtained by isolating microorganisms from soil, which decompose plant residue and more than half of which consisted of representatives of the genera Bacterium, Pseudomonas, Micrococcus and Bacillus. Cellulosolytic forms were referable to the genera Sporocytophaga, Cytophaga, Cellvibrio. The encountered fungus were representatives of Mucor and Penicillium. The formed community of microorganisms was preserved by means of periodic transfers to nutrient media where filter paper cellulose served as the only source of carbon [1].

Experiments dealing with degradation of wheat chaff were conducted in fermenters for continuous culturing of microorganisms. The process was run with aeration of the substrate at the rate of 1.5-2.0 ℓ/min air, using a mixer turning at the rate of 500 r/min and at a temperature of 22 and 36°C.

Wheat chaff (roots, stalks, husks) were first ground to 0.3-0.5 mm in size and suspended in 1 ℓ water. To this suspension we added a culture of cellulosolytic microorganisms in an amount of 5% of the fermenter volume, human urine serving as the source of nitrogen, used in an amount to provide a C:N ratio of 25:1; pH

the medium constituted 6.8-7.0 at the start of the process and 7.2-8.2 at the end. The experiments lasted 5, 10 and 20 days. The contents of the fermenters were centrifuged upon termination of the experiments. We measured dry mass, organic matter according to chemical oxygen uptake (COU) in sediment and cellulose content by the method of Kirshner and Ganek, as modified by A. V. Peterburgskiy [2] in the dissolved portion and sediment.

Results and Discussion

The data in Table 1 indicate that the effectiveness of the process increased proportionately to increase in duration of the experiment. During hydrolysis, some substances changed to a dissolved state and others were oxidized to CO_2 and water.

Table 1.
Dynamics of process of decomposition of wheat chaff at a temperature of 22°C

Duration of experiment, days	Decomposed substrate, % of initial mass	
	to CO_2 & H_2O	in solution
5	17.5±2.4	25.0±2.0
10	20.6±6.3	26.3±3.2
20	40.5±4.0	21.0±0.2

There was increased mineralization in the experiments conducted at a temperature of 36°C according to all parameters (Table 2). Moreover, in this case we observed more intensive change of organic matter into solution to 40% of the initial weight of the substrate.

Table 3 lists data obtained for decomposition of vegetable tops (beets, carrots and peas)

Table 2. Comparative results of the process of decomposition of wheat chaff at temperatures of 22 and 36°C in the course of 10 days

Temperature, °C	Amount of substrate broken down, % of initial mass		
	to CO_2 and H_2O	in solution	cellulose decomposed
22	20.6±6.4	26.3±3.2	27.5±1.4
36	30.2±12.0	40.8±8.0	38.5±9.4

Table 3. Results of biological decomposition of beet haulm, carrot and pea haulm and roots at temperature of 22°C for a period of 10 days

Substrate	Amount of substrate decomposed, % of initial mass		
	to CO_2 and H_2O	in solution	cellulose decomposed
Beet tops	51±6.5	29±3.0	48±5
Carrot tops and roots	51±5.0	19±1.8	65±6.5
Pea haulm and roots	54±8.0	17±2.0	--

We observed a considerably greater decomposition effect in the experiments than in wheat chaff over the same period of time (see Table 1).

We also measured experimentally the amounts of CO_2 and NH_3 discharged during decomposition of waste from plants raised in the greenhouse of the experimental complex (Table 4).

Table 4. Discharge of CO_2 and NH_3 during decomposition of greenhouse plant waste scaled per man per day

Substrate	Yield, g/day	Decomposed substrate, % of initial mass	Decomposed substrate yield, g/g	
			CO_2	NH_3
Wheat waste (straw, roots, chaff)	127	50±14	0.47±0.05	0.008±0.001
Vegetable waste (beets, carrots, peas)	7.61	54.9±0.5	0.8±0.01	0.0012±0.001

If we were to proceed from the stochiometric relations of the process of carbohydrate hydrolysis, there should be 1.62 g CO_2 output and 1.1 g O_2 uptake per gram organic matter from plant waste broken down to CO_2 and H_2O [3].

Table 4 shows that the experimental data on CO_2 output constituted 30% of estimated value in decomposition of wheat chaff and 50% in breakdown of vegetable waste.

Thus, in the experimental model of a biological life-support system, decomposition of greenhouse plant waste calculated per man per day should result in 66.8 g CO_2 output and 0.518 NH_3 output, with 45.3 g O_2 uptake.

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EFFECT OF SEX HORMONES ON SOME PARAMETERS OF CARBOHYDRATE METABOLISM IN THE LUNGS OF HYPOXIC RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 28 Oct 80) pp 45-48

[Article by N. N. Pribylova]

[English abstract from source] Experiments were carried out to reveal changes in the content of glucose, glycogen, pyruvate and lactate and in the activity of hexokinase and lactate dehydrogenase in the lungs of white rats exposed to 7- and 35-day hypoxia (rise to 9000 m for 6 hours daily) and treated with progesterone and testosterone. Treatment with the steroid hormones during chronic hypoxia increased the pulmonary content of glucose, glycogen, pyruvate, and decreased hexokinase activity and lactate accumulation.

[Text] Information about incretory function of reproductive glands in the presence of hypoxia is sparse [1-5]. It has been proven that there is depression of male reproductive and incretory functions of sex glands under hypoxic conditions [1-6]. Depressed production of androgens and progesterone, and increased production of estrogens has been noted in clinical internal medical practice in patients with chronic lung pathology and chronic hypoxia [7-11]. There are contradictory data in the literature concerning the effects of testosterone and progesterone on tolerance of hypoxia and pulmonary functions [3-5, 12, 13]. It was established in recent years that the lungs are the most important source of testosterone and progesterone metabolism [14-16]. Receptors have been discovered in the lungs for androgens and estrogens, and it has been proven that there is a special protein in lung tissue, uteroglobin, which resembles the protein in the uterus and which reacts to cortisol and testosterone [17]. The effect of hormones on carbohydrate metabolism under hypoxic conditions has not been sufficiently investigated [18-23]. Nor is there any information in the literature concerning the effects of sex glands on energy metabolism in the lungs under hypoxic conditions.

Methods

Experiments were conducted on 180 puberal male albino rats weighing 180-250 g. They were submitted to surgical castration under ether anesthesia. Hypoxia was produced by means of numerous "ascents" of the animals to an altitude of 9000 m for 6 h/day for 7 and 35 days, in a pressure chamber and by the method of A. A. Birkun and I. N. Nemirovskaya [24]. The animals were placed in the chamber 2 weeks

after castration. The animals were given testosterone or progesterone daily in a concentration of 1 mg/100 body weight for 7 (first group, 20 animals) and 35 (second group, 20 animals) days under hypoxic conditions.

As a control, we used 40 castrated and 40 intact rats submitted to hypoxia for 7 and 35 days, as well as 20 healthy rats kept under ordinary conditions. The animals were decapitated after 7 and 35 days of hypoxia.

The lungs were washed in cold water, dried on filter paper, weighed and homogenized at 0°C for 1-2 min in a Potter type glass homogenizer. The obtained 10% homogenate was used to assay glucose, glycogen, lactic and pyruvic acids, protein, activity of hexokinase and lactate dehydrogenase (LDH).

Glucose content was measured by the orthotoluidine method [25], protein by the biuret reaction [26], lactate according to Barker et al. [27], pyruvate concentration by the method of Umbreit [28], hexokinase activity by the method of Long [29] and LDH activity by the spectrophotometric method after Kh. M. Rubina et al. [30]. The obtained data were submitted to processing by the method of variation statistics.

Results and Discussion

There was drastic reduction of energy resources in rat lungs during 7-day hypoxia: reliable ($P<0.001$) decrease in concentrations of glucose and glycogen, depressed hexokinase and LDH activity, accumulation of lactic acid. Under the same conditions, castrated animals presented a distinctive temporary postcastration protective effect, directed at retention of glucose, glycogen and pyruvate in the lungs, and reduction of lactate ($P<0.001$) perhaps due to intensification of glucocorticoid function of the adrenals following orchiectomy. However, administration of testosterone to orchiectomied animals elicited more reliable accumulation in lung tissues of glucose, glycogen and reduction of lactate with increased LDH activity ($P<0.001$).

As can be seen in the Table, administration of progesterone for 7 days to castrated hypoxic animals had a less marked effect. Our findings coincide with the results obtained by other authors, who proved that testosterone and progesterone raise blood glucose level [20-23].

These hormones had an effect in the same direction on increase in LDH activity in the lungs and reduction of lactate concentration. Progesterone elicited a more marked decrease in hexokinase activity; however, this did not conform with the more distinct elevation of glucose level in lung tissue.

The results of these studies revealed that there were marked changes in carbohydrate metabolism under the effect of long-term hypoxic stress for 35 days, in the lungs of both intact and castrated white rats. The greatest changes in the parameters of carbohydrate metabolism studied were noted in the lungs of castrated males. They presented more marked accumulation of lactate in lung tissue, increase in lactate/pyruvate concentration ratio (to 17.8, versus 11.1 in intact males) and drastic increase in glycogen which increased significantly the death rate among castrated animals submitted to prolonged hypoxia (10 out of 20 rats), as compared to intact animals (4 out of 20 rats). Dissection of castrated rats that died of hypoxia revealed abscesses in the lungs of 3 out of 10 animals; all animals presented extensive hemorrhages in the lungs, dilatation and flaccidity of the heart.

Effect of testosterone and progesterone on main parameters of carbohydrate metabolism in the lungs of hypoxic rats

Animal group	Glucose, mg%	Glycogen, mg%	Lactate, mg%	Pyruvate, mg%	Hexokinase, μM/mg protein/min	LDH, μM/mg protein/min
			Control			
Intact	23,2±1,2	61,3±3,2	15,7±0,5	1,58±0,01	0,064±0,001	0,810±0,005
			7-day hypoxia			
Intact	6,8±0,2	21,4±0,3	45,9±0,4	1,87±0,04	0,021±0,003	0,430±0,001
Castrated	9,2±0,6	19,6±0,5	23,1±0,2	2,46±0,02	0,029±0,004	0,298±0,007
Castrated, given testosterone	16,4±0,4	34±0,5	10,0±0,2	1,64±0,003	0,038±0,002	0,390±0,010
Castrated, given progesterone	12,6±0,3	20±0,2	14,9±0,1	2,41±0,04	0,017±0,001	0,310±0,007
			35-day hypoxia			
Intact	14±0,1	10,2±0,2	23,8±0,1	2,15±0,01	0,027±0,001	0,550±0,005
Castrated	18,1±0,7	2,4±0,2	34,6±0,5	1,94±0,01	0,037±0,004	0,540±0,005
Castrated, given testosterone	18,5±0,5	20,7±0,6	14±1,7	0,88±0,01	0,012±0,001	0,120±0,001
Castrated, given progesterone	29,6±0,2	29,6±0,6	18,6±0,7	1,98±0,04	0,010±0,001	0,220±0,003

Long-term administration of testosterone and progesterone prevented the high death rate among castrated rats submitted to hypoxia for 35 days. Prolonged replacement therapy with testosterone during the 5 weeks of hypoxia caused greater build-up of glycogen and decrease in lactic acid, pyruvate, hexokinase and LDH.

Progesterone had an analogous activity, but hexokinase activity was more depressed, and this led to more marked accumulation of glucose in lung tissue. There was more marked production of pyruvate in response to progesterone, which perhaps was instrumental in synthesis of the surfactant system in the lungs [31, 32], particularly since prior studies revealed that there was maximum phospholipid production in the lungs under hypoxic conditions in response to administration of protesterone.

Thus, administration of steroid hormones (testosterone and progesterone) under hypoxic conditions led to increased accumulation of the main energy resources in the lungs--glucose and glycogen, decreased activity of hexokinase and diminished production of lactic acid, which improved tolerance of hypoxia by castrated rats when these hormones were given.

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EFFECT OF CHRONIC GAMMA IRRADIATION ON PROTEIN COMPOSITION AND CHOLESTEROL CONTENT OF CANINE BLOOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 2 Jan 80) pp 48-50

[Article by A. A. Akhunov]

[English abstract from source] In a chronic experiment dogs were exposed to irradiation in doses of 190, 360 and 560 rad for 3 years. As compared to the unirradiated controls they showed a slower recovery of the albumin and cholesterol content in the blood. The cholesterol content varied, depending on the dose of chronic irradiation, whereas the protein content did not show such a correlation.

[Text] Chronic exposure to ionizing radiation could lead to discrete functional disorders, which can be demonstrated in the presence of additional burdens [1]. We used bloodletting in this study for demonstration of possible latent changes. In the opinion of some researchers, bloodletting is a procedure that enhances and permits analysis of protein metabolic disturbances caused by radiation [2].

Methods

Three groups of dogs (6 in each group) were exposed to daily radiation from ^{60}Co sources in a dosage of 0.17 rad/day. The first group was submitted only to chronic irradiation; the second group was submitted to additional annual irradiation, once in a dose of 42 rad and twice in a dosage of 8 rad, against the background of chronic irradiation. The third group was exposed to 42 rad radiation 3 times at equal intervals in addition to chronic irradiation. The cumulative doses of radiation over the 3 years constituted 190, 360 and 560 rad, for the first, second and third groups, respectively. The fourth group consisted of nonirradiated dogs (control). The experimental conditions have been described in more detail in a previous report [3].

Upon termination of irradiation over a 3-year period, we tested the dogs with the use of an additional burden, bloodletting at the rate of 25 mℓ/kg body weight [4]. We assessed the reaction to bloodletting by the changes in blood serum total protein and protein fractions, as well as cholesterol. The biochemical parameters were measured before the load, then 1, 2, 5, 7, 12, 20 and 42 days after. Total blood serum protein was assayed by the refractometric method [5], protein fractions by electrophoresis on paper [6] and cholesterol by the method in [7]. We used the criterion of Student for statistical processing of the data.

Results and Discussion

At the early stages, irradiated and control dogs presented the same reaction to bloodletting. All groups of animals showed a decrease in protein and cholesterol content. Thus, 1 day after the load, there was a 1.0-1.6 g% decrease in total protein in the 4 groups, versus 7.4±0.1-7.8±0.2 g% as the base level ($P<0.05$). The decrease in protein content was referable to albumins and some globulin fractions. The most distinct change in albumin content was demonstrated in the third and fourth groups of dogs after 2 days, when it decreased by 0.9-1.0 g% versus 3.4±0.2 g% at the start ($P<0.05$). We failed to demonstrate appreciable changes in levels of α-1- and α-2-globulins. The dogs in the first group were an exception, since they presented 0.8±0.07 g% α-2-globulins, versus the initial level of 1.3±0.1 g% ($P<0.05$). At the same time, the amount of β-globulins did not change in the first group, whereas the level of this protein decreased by 0.4-0.5 g% from the base amount of 1.5±0.1-1.6±0.08 g% ($P<0.05$). The most appreciable change in γ-globulin content was noted in the second group of animals, where the level of this protein dropped to 0.5±0.06 g% ($P<0.05$) after 1 day, which constituted 45% of the initial value (0.9±0.1 g%). The decrease in γ-globulins was less marked (15-29%) in the other groups. As shown by the data in the Table, 1 day after bloodletting there was a 21.1 and 22.7% decline of cholesterol level in the first and fourth groups of animals, respectively, while the changes were less marked in the other two groups.

Effect of bloodletting on blood serum cholesterol level (mg%) in dogs submitted to chronic irradiation (M±m)

Day of study	Dose, rad			Control
	190	360	560	
Before bloodletting	171±13,4	190±11,2	218±9,4	150±13,2
1	135±5,4*	180±10,4	194±5,0	116±8,8
2	—	246±11,6*	208±18,7	167±12,0
5	210±11,2*	224±15,7	197±18,0	189±13,3
7	—	219±10,9	191±5,1*	233±9,0*
12	248±8,0*	203±12,3	191±4,9*	248±8,0*
42	179±8,0	189±10,0	165±9,3*	158±5,7

* $P<0,05$ as compared to data before bloodletting.

The demonstrated changes in blood biochemistry were unstable and reversible. A tendency toward normalization of protein levels was demonstrable already after 5-7 days. However, the recovery process was different in irradiated animals than in the control. Thus, after 12 days, all of the irradiated animals presented a second drop, by 15.7-26.5%, in albumin levels, whereas the tendency toward normalization persisted in control animals. Thereafter, albumin level rose again in the irradiated dogs, but remained 7-15% lower than the base level. At the end of the observation period, control animals presented 9% higher albumin level than the initial value, and it constituted 3.7±0.3 g%. With respect to nature of restoration of levels of α-1-, α-2- and β-globulins, the parameters of irradiated animals did not differ appreciably from the control. The amounts of these protein fractions reverted to normal 7 and 12 days after bloodletting. The nature of restoration of γ-globulins in the first group of dogs was the same as in the control. In the second and third groups of animals, normalization occurred in the same manner as in the control; however their γ-globulin levels were 14-22% higher ($P>0.05$).

Normalization of cholesterol level was the same in the first and second groups of dogs as in the control. There was an appreciable increase in cholesterol content in these animals 2 and 5 days after bloodletting, with return to base values after 42 days. It must be noted that hypercholesterolemia was less marked in the second group than in the first and fourth (see Table). However, the third group of dogs presented hypocholesterolemia at all tested times, and cholesterol level did not revert to normal, even at the end of the observation period.

The brief decrease in protein and cholesterol content after bloodletting was apparently due to loss of blood, whereas the subsequent increase was attributable to manifestation of the compensatory and recovery reaction [2, 8]. The slower recovery of cholesterol level in irradiated dogs (third group) and of albumins (first-third groups) was probably related to damage to some phases of synthesis in the liver or increased utilization thereof and destruction of tissues, which is also mentioned by other researchers [2, 8].

Thus, after bloodletting we demonstrated differences between irradiated dogs (doses of 190, 360 and 560 rad) and control animals, which had not been previously found without the additional burden. The differences consisted of slower normalization of changes induced by the burden in irradiated animals, as compared to the control. The incomplete recovery was probably related to attenuation of the compensatory-recovery reaction and depressed synthesis of albumins and cholesterol in the liver of irradiated dogs. We failed to demonstrate a clearcut relationship between changes in protein content and radiation dosage. However, the change in cholesterol content after bloodletting was related to dosage. The stable hypocholesterolemia with a dosage of 560 rad and normalization of cholesterol level with lower doses lead us to tentatively offer 190-360 rad as the threshold dosage with regard to this parameter in the case of chronic exposure to radiation for 3 years.

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EFFECT OF STATIONARY MAGNETIC FIELD ON THE THYROID

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 5 Mar 80) pp 50-52

[Article by V. M. Katola, A. D. Chertov, V. I. Kirichenko, A. B. Pirogov and V. I. Molchanov]

[English abstract from source] Rats were exposed to a constant magnetic field of 26268 A/m. Depending on the exposure time, the thyroid gland showed changes in the follicular epithelium height, content of ribonucleoproteins and PAS-positive substance, activity of adenylate cyclase, whereas blood serum exhibited changes in the concentration of thyroid hormones and no changes in the content of thyrotropic hormone.

[Text] This work deals with exploration of little-studied aspects of the effect of a stationary magnetic field (SMF) on endocrine function [1, 2].

Methods

Experiments were conducted on 46 mongrel male white rats weighing 170-200 g. Some of the animals were exposed for 30 min/day to a SMF of 26268 A/m without restricting their movements: first group (12 rats) for 2 days and second group (15 rats) for 7 days. All of these animals were decapitated 24 h after the last exposure, whereas the remaining 10 rats (third group) were sacrificed 21 days after 7-fold exposure to the SMF. Nine animals constituted the fourth, control, group (5 rats were sacrificed concurrently with the animals in the first group and 4 at the same time as the third group).

We fixed the thyroid in Carnoy fluid and imbedded it in paraffin. Histological sections were stained with Bemer's hematoxylin and eosin. In each instance, we measured the height of 100 thyrocytes using an MOV-1 ocular micrometer. Nucleic acids were studied according to Einarson and neutral polysaccharides according to Van Duyn. Adenylate cyclase (AC) was determined by the method of Rayk et al. [3] as modified by B. Ya. Ryzhavskiy [4]. The results were evaluated visually, according to amount and nature of distribution of the end product of the histochemical reaction--lead sulfide. The specificity of the reaction was proven by means of appropriate controls, which are mentioned in the original formula. We used the radioimmunological method [5] with test kits of the ByK-Mallincrodt Firm (FRG) for determination of blood serum concentration of thyrotropic hormone (TTH) of the anterior lobe of the hypophysis, total thyroxin (T_4), thyroxin-binding

capacity of serum proteins (T_3) and thyroxin efficiency coefficient (TEC). The value of the latter is proportionate to the amount of free thyroxin, and it reflects the intensity of cellular metabolism of thyroid hormones.

Results and Discussion

In intact rats, the thyroid is invested in a capsule, from which are given off some thin layers of connective tissue; however, there is insignificant expression of lobes. Right under the capsule there are large follicles, and their diameter decreases with distance from the capsule (the follicles are quite small in the middle of the gland). The mean height of thyrocytes is 7.8±0.2 μm. The thyrocytes contain a moderate amount of ribonucleoproteins and colloid PAS-positive substance. Adenylate cyclase is localized mainly in nerve fibers and endothelium of blood capillaries; the histochemical reaction is indistinct in the thyrocytes. It was quite difficult to determine whether the enzyme was present in the follicles also, since the observed accumulation of lead sulfide in their central part (so-called central granule) could be elicited by a number of other causes.

Effect of SMF on functional state of the thyroid and TTH level in blood serum of white rats

Animal group	T_3, relat. units	T_4, μg%	TEC relat. units	TTH, ng/mℓ	Ht. of follic. epith., μm	Levels of		AC activity
						Ribo-nucleo-proteins	PAS-positive subst.	
1 (n=12)	0.89±0.02 ($P>0.10$)	6.7±0.35 ($P<0.001$)	0.89±0.02 ($P<0.001$)	2.3±0.36 ($P>0.10$)	7.1±0.17 ($P<0.05$)	Low	High	High
2 (n=15)	1.0±0.14 ($P>0.10$)	11.3±0.8 ($P>0.10$)	1.0±0.02 ($P>0.10$)	2.7±0.34 ($P>0.10$)	8.2±0.1 ($P>0.10$)	Moderate	Low	Moder.
3 (n=10)	0.90±0.06 ($P>0.10$)	7.7±0.28 ($P<0.001$)	0.95±0.01 ($P<0.001$)	3.0±0.17 ($P>0.10$)	6.2±0.1 ($P<0.01$)	Low	High	High
4 (n=9)	0.92±0.04	10.4±0.5	1.08±0.03	3.04±0.27	7.8±0.2	Moder.	Moder.	Moder.

Note: P is given in relation to intact animals (4th group)

The Table shows the dynamics of morphological and histochemical changes in hormonal activity of the thyroid as related to frequency of exposure of rats to the SMF. It indicates that the height of the follicular epithelium and ribonucleoprotein content thereof diminished in the thyroid of the first group of animals. Follicular colloid became thicker and more oxyphilic with increase in amount of PAS-positive substance. There as activation of AC in nerve fibers and endothelium of blood capillaries, whereas the background stain of thyrocytes did not differ from the control. In most cases, the described changes were indicative of depressed hormonal activity of the thyroid, as confirmed by the low values for T_4 and TEC, with unchanged T_3, in blood serum. Concurrently, there was a decrease in TTH concentration, but the differences were statistically unreliable.

Longer exposure to the SMF (second group of rats) normalized the condition of the thyroid: the follicular epithelium was somewhat taller than in the control, ribonucleoprotein content reached the base level, there was a decrease in amount of PAS-positive substance and oxyphilia of colloid, with appearance of resorption vacuoles along the periphery of the latter. AC activity, concentrations of TTH, T_4,

T_3 and TEC showed virtually no difference from the corresponding control values. But, 3 weeks after discontinuing exposure to SMF, there was another inhibition of morpho-functional state of the thyroid (third group), analogous to what was demonstrated in the first group of rats.

According to the foregoing, there are phasic fluctuations in thyroid function of healthy rats, depending on the time of exposure to the SMF: initial inhibition was followed by normalization, with subsequent decrease in function, which was no longer directly attributable to the SMF. On the whole, these findings resembled the changes inherent in the thyroid under the influence of stress-producing stimuli.

When we analyzed this reaction, we were impressed by the fact that during exposure to the SMF there was no impairment of thyroxin binding by serum proteins; however, there was appreciable fluctuation of thyroid hormone levels with virtually stable thyrotropin level in serum. As we know, any change in concentration of thyroid hormones in blood leads, according to the feedback principle, to certain changes in pituitary hormonopoiesis [6]. For this reason, it is quite likely that exposure to the SMF either attenuated sensitivity of the thyroid gland to TTH, or provided for predominant regulation of its function via the parahypophyseal route. We cannot rule out the direct effect of the SMF.

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MECHANISM OF ADRENOSYMPATHETIC SYSTEM REACTION TO SINGLE EXPOSURE TO VARIABLE MAGNETIC FIELD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 10 Jul 80) pp 52-56

[Article by S. A. Sakharova, A. I. Ryzhov and N. A. Udintsev]

[Text] It was previously demonstrated [1, 2] that a variable magnetic field (VMF) of 200 Oe, 5 Hz is a stress factor in the case of 1-day exposure, under the influence of which activity of all parts of the adrenosympathetic system (ASS) increases. In view of the complex nature and functional correlation between the ASS and central nervous system, glucocorticoid function of the adrenals and catecholamine (CA) reserves, we investigated the role of these relationships in formation of the response of the ASS to a VMF.

Methods

Phenobarbital (80 mg/kg intraperitoneally) was used to exclude the central nervous system. Rausedyl [reserpine] (3 mg/kg subcuntaneously) was used to mobilize reserve catecholamines; dexasone (2 mg/150 g for 10-12 days intraperitoneally) induced compensatory atrophy of the adrenal cortex; after splanchnotomy, visible vessels and the lipid capsule were swabbed with 8% formalin. Animals were used in the experiment on the 8th day, when they developed signs of adrenal insufficiency. Rats given saline or 1% starch ash, as well as laparotomied animals, served as a control.

We assayed CA in the heart, liver, spleen, hypothalamus, brain stem and adrenals; epinephrine and norepinephrine [3-5] were assayed in the blood of 200 male rats weighing 150 g; we studied the morphological changes in organs after fixing them in Carnoy fluid, staining sections with eosin and hematoxylin, azan according to Heidenhain and others. The drugs were given to animals before putting them in a magnetic field of 200 Oe, 50 Hz for 1 day. The rats were decapitated immediately after removal from the VMF. VMF was created with a magnet having a trapezoid tip (top base 220 m, bottom base 275 mm, side 220 mm, height of magnet clearance 80 mm). The capacitive battery consisted of 6 type IM-3-100 condensers, with capacity of 110 μF and voltage of 3 kV. The magnet was powered by a ferromagnetic stabilizer with input voltage of 220 V. The magnet generated a 200-Oe VMF, with 50 Hz frequency, gradient of 1 Oe/cm and 12 A current in the coils.

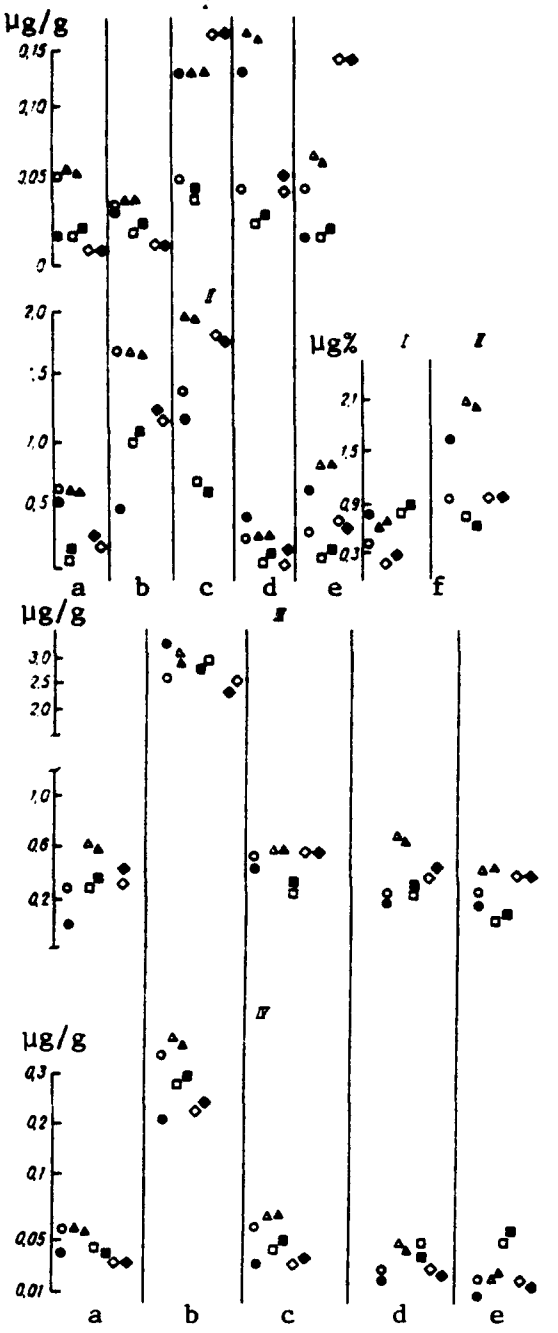

Figure 1.
Epinephrine (I), norepinehprine (II), dopamine (III), dopa (IV) levels in organs (µg/g) and blood (µg%) of white rats. White circles--control, black--VMF; white triangles--phenobarbital, black--phenobarbital + VMF; white squares--rausedyl, black--rausedyl + VMF; white rhombs--splanchnotomy, black--splanchnotomy + VMF

a) brain stem
b) hypothalamus
c) heart
d) liver
e) spleen
f) blood

Results and Discussion

Phenobarbital elicited prolonged sleep in healthy animals and caused accumulation of CA in tissues and blood (Figures 1 and 2): epinephrine in the heart and liver, norepinephrine in the heart and blood, dopamine in the brain stem and liver. There were morphological changes in the heart (drastic dilatation of capillaries, dyschromism of myocyte nuclei, marked perivascular edema, deformity and swelling of myocyte nuclei) and liver (dilatation of sinus capillaries, stasis, impaired architectonics of lobular cells).

Against the background of phenobarbital, the VMF did not elicit appreciable changes in CA content. The morphological changes in organs with exposure to VMF against the background of phenobarbital were typical for this physical factor, but they were more marked, particularly in the brain where the number of glial cells was increased near some neurons. Isolated neurons appeared with signs of tigrolysis and nuclei shifted to the periphery (Figure 3). Phenobarbital-induced exclusion of central regulatory mechanisms could have been the cause of these changes. Nor can we rule out the direct effect of the field on the central nervous system, which is characterized by marked sensitivity to magnetism. [6].

Administration to intact animals of rausedyl (see Figures 1 and 2) elicited depletion of tissular CA reserves, which corresponded to the reports of a number of authors [7-9]. The morphological changes in the heart, liver and spleen were insignificant. In the brain stem, there was a neuroglial reaction near some neurons. Some cells of the fascular region of the adrenals and, less often, of the reticular zone presented cytoplasmic vacuolization and, in a few cases, impairment of cytoarchitectonics.

Exposure of rats given rausedyl to VMF did not alter the CA content of tissues.

After denervation of the adrenals, there was a decline in levels of epinephrine and norepinephrine in the brain stem and

hypothalamus, as well as of norepinephrine in the liver; monoamine content of the adrenals diminished. On the other hand, there was an increase in epinephrine in the spleen, epinephrine and norepinephrine in the heart. In the opinion of a number of researchers [10-13], these findings are indicative of redistribution of CA in tissues.

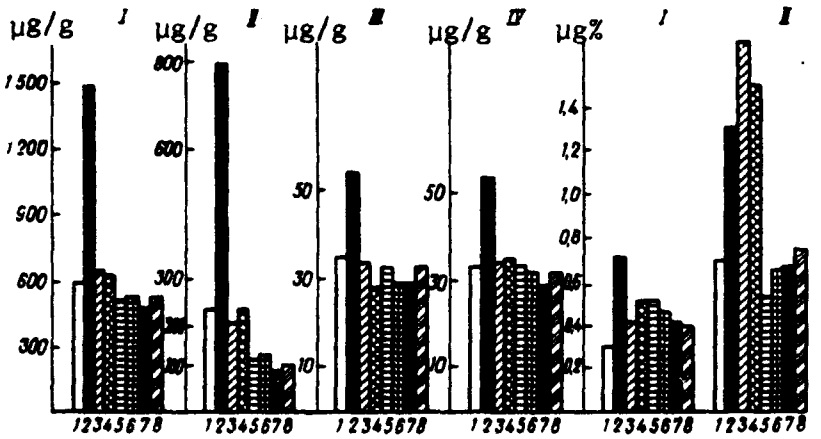

Figure 2. Catecholamine and dopa content of adrenals (g/g), epinephrine and norepinephrine content in blood (μg%) of white rats

I) epinephrine
II) norepinephrine
III) dopamine
IV) dopa
1) intact animals
2) VMF
3) phenobarbital
4) phenobarbital + VMF
5) rausedyl + VMF
6) rausedyl
7) splanchnotomy
8) splanchnotomy + VMF

Stasis, pyknosis of fascicular zone cell nuclei, deformation of cells of the capillary endothelium, regional dyschromia, perivascular and pericellular edema were demonstrated in the adrenals. There was a profusion of amorphous clumps in the lacunae of the medullary substance, most probably of a protein nature. The erythrocytes in lacunae were lighter and vaguely circumscribed. In leukocytes, chromatin was situated near the nuclear membrane. Azan staining showed light blue erythrocytes in the lacunae, whereas they were orange-red in intact denervated animals. A change in color of erythrocytes was also noted in other organs, but it was less marked; the changes in the heart were similar to those observed in the experiments with phenobarbital.

VMF against the background of splanchnotomy did not elicit additional changes in CA content or structural characteristics of organs. Consequently, the hormonal part of the ASS plays a substantial role in the reaction of this system to VMF.

After administration of dexasone, which elicits compensatory atrophy of the adrenal cortex, there was more than 30% reduction of its mass, decrease in epinephrine and norepinephrine content of the brain stem, adrenals and blood, epinephrine, dopamine in the hypothalamus, dopa in the adrenals, as well as accumulation of norepinephrine in the hypothalamus and of dopa in the brain stem (see Table).

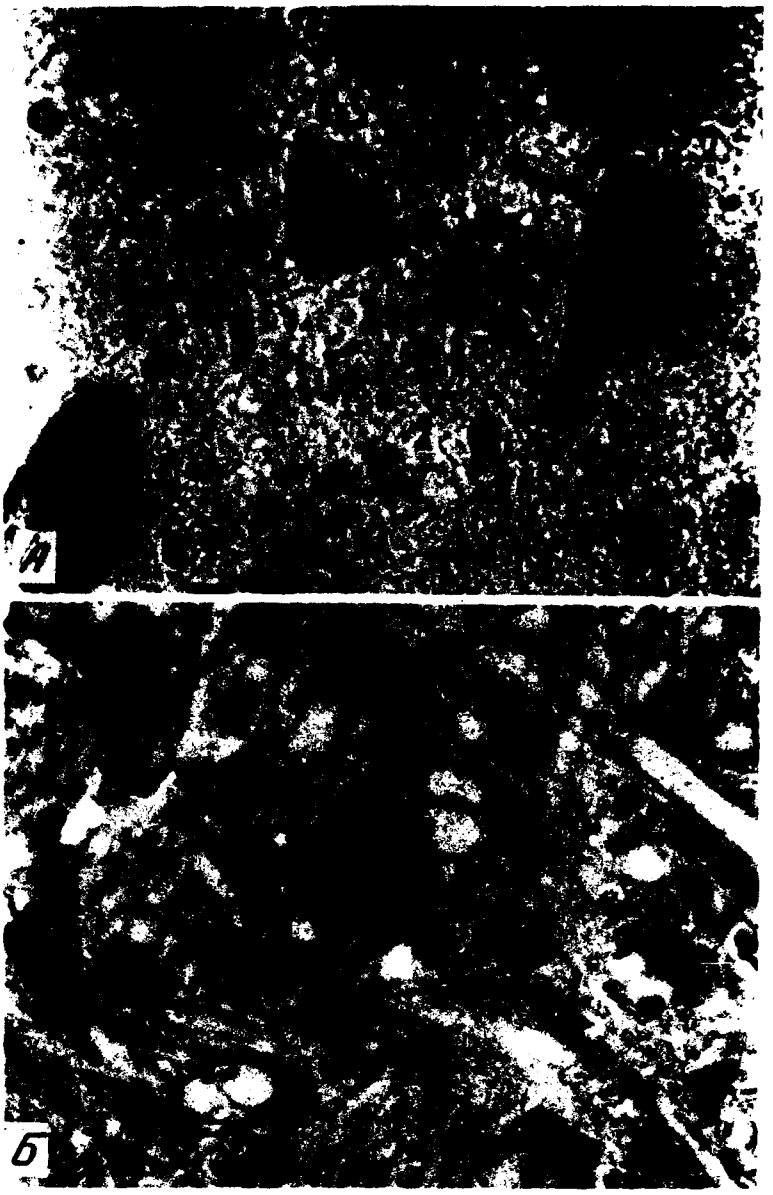

Figure 3. Brain of control rat (A) and after VMF and phenobarbital (Б). In the experimental specimen: tigrolysis, pyknosis of nucleus and migration thereof to the periphery of the neuronal body. Nissl staining; magnification 900×

Morphological examination revealed the greatest changes in the adrenals (drastic reduction of thickness of cortical layer of the adrenal and impairment of cyto-architectonics, chromatolysis in cell nuclei of the fascicular zone) and brain, where some neurons presented enlargement of granules of Nissl's substance and

occasionally tigrolysis. There were enlarged polynuclear cells in the hepatic lobes. The nuclei were clear in some hepatocytes, with drastically reduced chromatin content, dilated sinus capillaries and, in endothelial cells, hyperchromic nuclei. In the heart, there was perivascular edema and disappearance of transverse striation of myocytes. The nuclei of some cells were hyperchromic. Enlargement of malpighian bodies was observed in the spleen. There was a drastic increase in quantity of agranulocytes in red pulp.

CA and dopa content of organs (g/g) and blood (g%) of white rats (n = 8) exposed to VMF against the background of dexasone

Organ	Parameter	Animals			
		intact	VMF	dexasone	dexasone and VMF
Brain stem	Epinephrine	0,05±0,001	0,01±0,001*	0,0009±0,0001*	0,40±0,05
	Norepinephrine	0,6±0,03	0,59±0,05	0,33±0,05*	0,10±0,05*
	Dopamine	0,3±0,02	0,05±0,009*	0,24±0,06	0,20±0,02
	Dopa	0,05±0,001	0,04±0,005	0,20±0,002*	—
Hypothalamus	Epinephrine	0,02±0,005	0,02±0,003	0,001±0,0001*	—
	Norepinephrine	1,60±0,09	0,51±0,07	2,0±0,5*	0,40±0,05
	Dopamine	2,50±0,3	3,60±0,5*	0,93±0,05*	3,25±0,20*
	Dopa	0,3±0,02	0,12±0,04*	0,23±0,03	0,11±0,015*
Heart	Epinephrine	0,06±0,01	0,12±0,03*	0,07±0,01	0,06±0,01
	Norepinephrine	1,32±0,30	1,22±0,33	0,20±0,03*	1,18±0,02
	Dopamine	0,50±0,10	0,45±0,09	0,42±0,05	0,41±0,04
	Dopa	0,06±0,001	0,06±0,001	0,06±0,001	0,05±0,001
Liver	Epinephrine	0,05±0,001	0,12±0,02*	0,05±0,003	0,07±0,02
	Norepinephrine	0,12±0,04	0,22±0,03*	0,13±0,01	0,14±0,04
	Dopamine	0,15±0,04	0,16±0,05	0,14±0,01	0,17±0,02
	Dopa	0,02±0,001	0,02±0,003	0,02±0,001	0,02±0,001
Spleen	Epinephrine	0,05±0,001	0,01±0,001*	0,06±0,001	0,06±0,001
	Norepinephrine	0,30±0,03	0,45±0,03*	0,20±0,015	0,16±0,03
	Dopamine	0,20±0,01	0,20±0,08	0,23±0,030	0,19±0,04
	Dopa	0,02±0,001	0,10±0,015*	0,02±0,001	0,02±0,001
Adrenals	Epinephrine	612,0±83,8	1560,0±160,8*	512,8±63,8*	864,2±98,6*
	Norepinephrine	238,0±60,3	900,0±108,0*	32,7±8,3*	108,7±30,8*
	Dopamine	36,5±3,4	55,0±10,6*	32,3±3,3*	101,6±18,6*
	Dopa	33,2±2,6	53,0±8,2*	9,2±1,8*	71,2±20,1*
Blood	Epinephrine	0,4±0,09	0,78±0,05*	0,25±0,02*	1,52±0,2*
	Norepi-nephrine**	0,8±0,01	1,30±0,11*	0,35±0,1*	0,36±0,08

*$P \leq 0,05$ as compared to parameters of intact animals.
**We used 12 animals for the blood analyses.

In the presence of compensatory atrophy of the cortex, VMF elicited activation of central and hormonal parts of the ASS: decrease in epinephrine and dopamine in the brain stem, norepinephrine and dopa in the hypothalamus, accumulation of dopamine in the latter, epinephrine in blood and increase in the adrenals of all monoamines. The CA level in the heart, spleen and liver did not differ appreciably from the level in animals given dexasone.

The structural distinctions of the hypothalamus, brain stem and adrenals were the same as under the influence of dexasone alone. After exposure to VMF, there was significant disappearance of the dexasone-induced changes in the heart, liver and spleen.

Consequently, glucocorticoids play an appreciable role in the reaction of the mediator mediator part of the ASS to VMF.

Thus, the reaction of the ASS to VMF was absent in the experiments where phenobarbital and rausedyl were administered and splanchnotomy performed, whereas with administration of dexasone only the mediator part was not involved in the reaction. The experiments with phenobarbital and denervation of the adrenals warrant the belief that there is a neuroreflex mechanism in the reaction of the ASS to VMF; the experiments with rausedyl demonstrated that the CA reserve levels in organs play an important role in formation and degree of ASS reaction to the stressor, whereas the hemodynamic and morphological changes in cellular elements of organs induced by the field were related to mobilization of reserve CA in response to the VMF.

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EFFECT OF ATTENUATED GEOMAGNETIC FIELD ON E. COLI RESISTANCE TO ULTRAVIOLET RAYS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 19 Jan 79) pp 57-58

[Article by O. A. Alferov and T. V. Kuznetsova]

[English abstract from source] The effect of an attenuated geomagnetic field on E. coli tolerance to ultraviolet irradiation was studied. The geomagnetic field was shielded to provide 40- and 160-fold attenuation. It was demonstrated experimentally that the 160-fold attenuated field increased E. coli tolerance, whereas the 40-fold attenuated field decreased it. The geomagnetic effect depended on the exposure time, reaching maximum after five passages of E. coli. An additional magnetic field simulating the geomagnetic field generated in the shielded chamber reversed the effect of an attenuated geomagnetic field.

[Text] The sparse data in the literature indicate that an attenuated geomagnetic field (AGMF) retards growth of Staphylococcus aureus [1], Azotobacter and yeast [2]. It was also shown that, when cultivated in an AGMF [3], there is increased growth of E. coli CA-23, with loss of its capacity to ferment maltose and faster development of antibiotic resistance.

We submit here data on the effect of AGMF on E. coli resistance to UV [ultraviolet] rays and dependence of the observed effect on intensity and duration of exposure to AGMF.

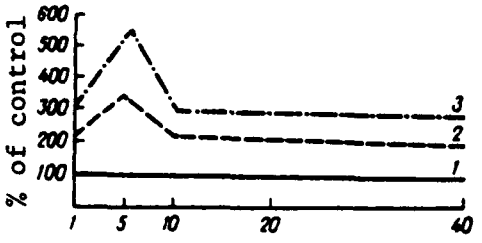
Methods

E. coli 0111 served as the object of our study. The AGMF was produced by means of shielding earth's magnetic field with iron cylinders, which attenuated it by 160 and 40 times. In order to eliminate residual technological voltage arising in the cylindrical shields when submitted to mechanical treatment and to improve the homogeneity of magnetic properties of the cylinder material, the cylinders were fired in a muffle furnace at 900°C for 5 h, then cooled to room temperature for 24 h together with the furnace. The residual magnetic field in the cylindrical shields constituted, according to estimates [4] and direct measurement, $(200\text{-}300)\cdot 10^{-5}$ and $(1100\text{-}1500)\cdot 10^{-5}$ Oe, changing in accordance with variations of the geomagnetic field (GMF). The method for preparing the cylindrical shields and measuring AGMF was described previously [5-8].

Suspensions in saline (50,000 bacterial bodies/mℓ suspension) were prepared from control and experimental cultures. The suspensions were exposed to UV for 20 and 40 s, BUF-2 lamps situated 50 cm away from the irradiated suspension serving as the UV source. The irradiated bacterial suspensions were plated in amounts of 0.1 mℓ in Petri dishes with beef-peptone agar. They were incubated at 37°C. We counted the number of colonies after 24 h. UV radiation was delivered in the absence of direct light. After exposure to UV, the cells were also kept in the dark.

Results and Discussion

As shown by the results of the first series of experiments (28 tests), a 160-fold attenuated GMF increased reliably the resistance of E. coli to UV, by 133% when exposed for 20 s and by 211% when exposed for 40 s. However, with 40-fold attenuation of the GMF, we observed the opposite effect: reliable decrease in E. coli resistance to UV by 40% with exposure for 20 s and 50% when exposed for 40 s.



Effect of 160-fold attenuated geomagnetic field on resistance of E. coli to UV light. X-axis, number of passages
1) control
2) exposure to UV for 20 s
3) exposure to UV for 40 s

In the second series (80 experiments) we studied the dependence of the demonstrated effect on duration of exposure to AGMF. For this purpose, we submitted experimental E. coli to daily passages in AGMF and control specimens in GMP, 5, 10, 20 and 40 times (see Figure).

As can be seen in this Figure, the effect was related to exposure time. It was the most marked after the fifth passage, when resistance increased by 206% with exposure for 20 s and by 419% with exposure for 40 s ($P<0.05$). After the 10th passage of bacteria in AGMF, there was 101% increase in resistance to UV with 20-s exposure and 131% increase with 40-s exposure ($P<0.05$), as compared to the control. E. coli resistance to UV held at the same level on the 20th and 40th days.

The demonstrated effects are, in our opinion, attributable solely to attenuation of GMF, and not to changes in experimental conditions referable to shielding of other fields (radio fields, radioactive background, solar radiation, UV rays, infrared fields, etc.). To confirm this, we generated a magnetic field within the cylindrical shield equal in value and direction to the GMF. The test was a change in E. coli resistance to UV light in the AGMF. We conducted 16 experiments, the results of which demonstrated that generation of a magnetic field in the shield equal to the GMF eliminated entirely the effect obtained with AGMF.

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EFFECT OF FLIGHT ABOARD COSMOS-936 BIOSATELLITE ON CONTRACTILE PROPERTIES OF RAT MUSCLE FIBERS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 6 May 80) pp 58-61

[Article by V. S. Oganov, S. A. Skuratova and M. A. Shirvinskaya]

[English abstract from source] Contractile properties of glycerinated fibers of skeletal muscles of rats flown for 18.5 days on Cosmos-936 were investigated. In slow antigravitational muscles (soleus m. and triceps brachii m.), decrease in the amplitude of isometric tension and performance as well as acceleration of the contraction development were observed. The studies point to a high specificity of reactions of skeletal muscles to the experimental conditions, depending on their functional specialization. It is suggested that changes in contractile properties of myofibrillar proteins may contribute to the adaptive rearrangement of functional properties of antigravitational muscles under the influence of space flight.

[Text] Signs of functional atrophy of muscles and adaptive transformation of their contractile properties after a 20-22-day space flight could reflect not only certain changes in their structure [1] and some elements of metabolism [2, 3], but changes in contractile properties of myofibrillar proteins proper.

To test this hypothesis, we studied here contractility of glycerinated muscle fibers, since we know that preglycerination, which partially destroys sarcolemma and flushes several metabolic substrates from muscle fibers, preserves the native organization of myofibrillar proteins and their capacity for ATP hydrolysis and contraction [4].

Methods

We studied the muscles of the hind legs--soleus (SM) and extensor digitorum longus (EDL), and of the front legs--medial head of the brachial triceps (MHBT) and brachial muscle (BM). We obtained the material for our studies from decapitated animals in the flight group (FG), ground-based synchronous experiment (GG) and vivarium control (VC) 5-9 h (first time--I) after termination of an 18.5-day flight aboard Cosmos-936 biosatellite [5] and control experiments. We also examined the MHBT and BM preparations obtained from animals 25 days after the space flight (second time--II).

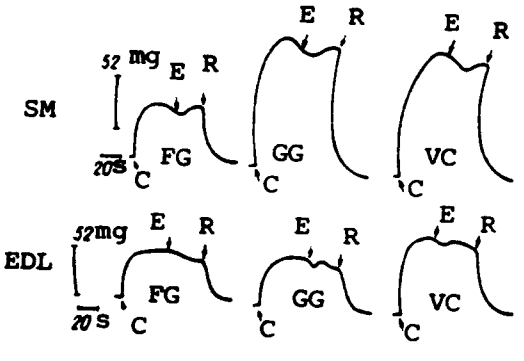
We treated the muscles with glycerine by the method of Szent-Gyorgyi [6] as modified in [7-9] and in our modification, for which purpose, the muscle preparations, which were fixed in relaxed position, were placed in a 50% glycerin solution with 10 mM ethylenediaminotetraacetic acid (EDTA), keeping them at 0°C and pH 7.0 for 24 h, with frequent stirring. The muscles were then transferred to fresh solution containing 10 mM EDTA, 50% glycerin and 0.067 M standard phosphate buffer, and then stored until needed at -18°C for 4-6 months.

For our studies, we isolated 15-40 fasciles containing 2-7 fibers from each sample of glycerinated muscle tissue. Such preparations contracted under isometric conditions when placed in a solution containing 5 mM ATP, 5 mM $MgCl_2$ and 0.15 mM CaCl [4]. To inactivate the preparations, they were eluated in buffered solution of KCl (0.03 M KH_2PO_4 + 0.05 M KCl) and transferred to a relaxing solution (0.1 M KCl, 7 mM $MgCl_2$ + 5 mM ATP + 4 mM EDTA + 20 mM histidine) [9]. We performed these manipulations at room temperature and pH 7.2.

Before making physiological measurements, we determined the mean diameter of each fiber in a fascicle (under a microscope using an ocular micrometer) and calculated its cross section. To measure the parameters of contraction of the preparation in an isometric system, we used a type 6MKh1B mechanotron as sensitive element and a mechanoelectric converter. We recorded the contraction process by means of an ink-tracing milliammeter (see Figure). In processing the tracings, we measured tension (maximum amplitude, P_{max}, in grams/mm^2 area of fiber cross section). We also calculated the area under the curve of development of isometric tension circumscribed by the time P_m was reached. This parameter (grams/s/fiber)--"force impulse" by definition-- was arbitrarily (in the situation without shifting of working point) as the gauge of efficiency [work capacity]. Reliability of differences between parameters was assessed by the method of Student-Fisher.

Results and Discussion

There are few data in the literature concerning contractility of glycerinated muscle fibers of warm-blood organisms. Nevertheless, we should mention that our data on the value of isometric tension of glycerinated muscles of intact rats conform well with those in the literature [7, 8, 10].



Samples of tracings of isometric contraction of preparations of glycerinated fibers from fast and slow muscles. C, E and R--contracting, eluating and relaxing solutions, respectively

The results of our studies as a whole indicate that the type of reaction of the contractile system of different muscles to space flight factors is determined, to a considerable extent, by the functional specialization of the muscles and biomechanical conditions of contraction thereof.

The greatest changes were demonstrated in the SM (one of the most active antigravity muscles), which consists chiefly of intermediate and slow fibers [11]. Isometric tension of SM fibers in FG rats diminished reliably, as compared to the GG and VC animals (Table 1).

Table 1.
Maximum isometric tension of glycerinated muscle preparations (g/mm^2)

Muscle	Time	Group		
		FG	GG	VC
SM	I	15.43±13.18** (4:100)	27.86±3.17 (5:141)	24.24±2.29 (5:126)
EDL	I	14.44±2.22 (5:86)	13.95±1.41 (5:71)	16.55±1.98 (5:80)
	I	18.75±2.25** (5:96)	26.74±4.20* (5:96)	14.33±1.57 (6:96)
MHBT	II	17.54±1.52 (5:120)	14.58±1.69 (6:121)	14.18±2.10 (7:110)
	I	23.09±2.22 (5:113)	19.37±2.36 (5:109)	12.30±1.68 (7:146)
BM	II	16.53±1.98* (5:128)	13.62±2.91 (5:109)	10.93±0.85 (10:148)

Table 2.
Force impulse of glycerinated muscle preparations in isometric contraction (ns)

Muscle	Time	Group		
		FG	GG	VC
SM	I	161.97±43.59** (4:100)	577.00±74.50 (5:141)	589.45±49.83 (5:126)
EDL	I	240.96±33.88 (5:86)	292.30±54.25 (5:71)	216.30±36.15 (5:80)
	I	192.17±37.54** (5:96)	367.22±63.05 (5:86)	248.30±22.57 (6:96)
MHBT	II	175.22±6.52 (5:120)	167.34±15.86 (6:121)	170.58±15.31 (7:110)
	I	214.69±40.50* (5:113)	172.09±31.37* (5:116)	97.19±22.99 (7:146)
BM	II	185.16±25.42 (5:128)	169.49±28.71 (5:109)	139.47±15.82 (10:148)

Note: In both tables, ratio of number of rats used to number of preparations obtained is given in parentheses. One asterisk indicates statistically reliable differences in relation to VC group; two asterisks indicate the same in relation to GG and VC groups.

Isometric tension of MHBT was also lower in FG rats than in GG. At the same time, it was higher in both of these groups than in the VC group; however, this difference was not statistically reliable for the FG rats (see Table 1). As can be seen in Table 2, there was more marked decline of "efficiency" of SM preparations (according to force impulse parameter) than reduction of force of contraction. Unlike the tension amplitude in GG and VC rats, in the FG this parameter for MHBT was reliably lower, but its level showed virtually no difference from control values 25 days after the flight (see Table 2). As can be seen in Tables 1 and 2, there were no statistically significant changes in contraction amplitude or force impulse in EDL preparations from animals of all three groups. In contrast, we demonstrated an increase in amplitude of contraction and force impulse in the fast muscle of the foreleg, the BM, in FG and GG animals, as compared to VC. Only the amplitude of contraction of BM preparations from FG rats remained high 25 days after the flight (see Table 1).

It is known that the time of the contractile act is more subject to the effects of such experimental conditions as ATP concentration, rate of its diffusion to the active myosin centers in this model than the force parameters, and this in turn is related to the size of the preparations, number of fibers, etc. [4]. Since this makes it difficult to perform a comparative quantitative analysis of the rate of contraction of preparations of different muscles, we used the time of development of contraction over an empirically selected linear segment of the curve (P_{max} 0.2-0.6) for qualitative [or satisfactory?] evaluation thereof. This parameter was standardized according to minimum value of P_{max} in all preparations.

After the space flight we demonstrated a distinct tendency toward reduction of time of development of isometric tension in SM preparations and the opposite tendency in EDL preparations. Immediately after the flight, this parameter of muscles of the foreleg showed virtually no change; however, after 25 days of readaptation these muscles presented a mild tendency toward reduction of time of development of tension.

Studies conducted previously (Cosmos-605 and Cosmos-690 biosatellites) also revealed a decrease in force of contraction, work capacity [efficiency] (resistance to fatigue) and acceleration of the process of development of tetanic contraction in a whole SM preparation [12]. On the basis of the results of the present study, it can be assumed that the process of adaptation of skeletal muscles having a marked antigravity function to weightlessness is most probably associated with appropriate changes in contractile properties of myofibrillar proteins. The latter may be related to certain structural changes in contractile and regulatory muscular proteins. There are data, for example, indicative of alteration of the subunit composition of troponin in the posterior crural muscle group in an experiment conducted aboard the Cosmos-605 biosatellite [13].

The results obtained on preparations of the other muscles studied were not as unequivocal. The changes demonstrated in them are most likely derived from interaction of the effects of weightlessness and upkeep conditions. Their manifestations are different in different muscles, and they are related to structural and functional specialization thereof, as well as the nature of possible changes in biomechanics of contraction of a given muscle under experimental conditions.

Thus, one would think that some conditioning of the MHBT occurred in the synchronous experiment due to a change in biomechanical conditions of foreleg function in a small space in rats adapted to differentiated movements. Evidently, the space flight eliminates this effect. At the same time, the same decline of work capacity occurs in the MHBT of the FG animals as in the SM, in the absence of overt signs of atrophy.

As shown by the results of our study, no appreciable changes in contractile properties of glycerinated fibers were demonstrated after the space flight in the fast EDL muscle, which is similar in fiber composition to the MHBT, but is less involved in postural activity [14]. Analogous results were obtained in the experiment aboard Cosmos-605 biosatellite [15]. Our findings here warrant the assumption that the insignificant changes in contractile properties of preparations of whole EDL muscles previously demonstrated (Cosmos-605 and Cosmos-690 biosatellites)[12] are more related to animal upkeep conditions, in particular, relative hypokinesia, than directly to weightlessness.

Unlike the muscles of the hind leg and MHBT, the parameters of force and work capacity of the fast brachial muscle were reliably higher than in the control. It can be assumed that this somewhat unexpected increase in functional capacity of the BM is the result of conditioning thereof due to the increased activity of foreleg muscles. The latter, as we have noted, are adapted in rats for finely differentiated movements and, perhaps, are used by the animals to stabilize the position of the body in unsupported space [16]. The data indicative of increase in overall level of motor activity of animals in flight indirectly favor this hypothesis [17].

Thus, the results of the present study provided convincing confirmation of the high specificity of reactions of some skeletal muscles to space flight conditions, and this is apparently attributable to the unique fiber composition of each muscle because of the high degree of their functional specialization. Moreover, it was shown that corresponding changes in contractile properties of myofibrillar proteins apparently play some role in the aggregate of changes in basic characteristics of contraction, which develop in slow antigravity muscles under the influence of space flgiht. These changes in myofibrillar proteins may be attributable to some

degree of transformation of the structure, subunit composition and physicochemical characteristics of protein macromolecules. This question, which is very important from the theoretical and practical points of view, requires special investigation.

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ARTIFICIAL GRAVITY AS A MEANS OF PREVENTING ATROPHIC SKELETAL CHANGES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 3 Mar 80) pp 62-63

[Article by G. P. Stupakov]

[English abstract from source] It has been demonstrated that exposure of rats to artificial gravity of 1 g onboard the biosatellite Cosmos-936 can prevent development of osteoporosis in them.

[Text] Development of osteoporosis under the influence of factors associated with long-term space flights has been demonstrated in the human calcaneus [1] and spongiform parts of rat long bones, which was associated with substantial reduction of parameters of bone strength in these animals [2]. There has been no experimental confirmation of the possibility of preventing atrophy of osseous tissue during space flights.

Our objective here was to test the efficacy of artificial gravity (AG), created by an onboard centrifuge in the Cosmos-936 biosatellite, as a means of preventing development of osteoporosis in weightlessness.

Methods

The experimental conditions were described in detail in a previously published work [3].

We assayed the mineral component in the proximal epimetaphyseal region of fresh, skeletized rat tibias (5 bones from 5 animals in each group) by the method of direct photo absorptiometry, measuring their weight and volume also. Absorptiometry was performed by means of a Studsvik (Sweden) Bone Scanner 71Q2, with the radioisotope, ^{245}Am.

Each bone was scanned in air four times, and we determined the average reading (mean-square error did not exceed 4%). The results were expressed in grams of hydroxyapatite per square cm of scanned area.

We determined the volume of the entire bone by weighing it in air and water. Weighing error did not exceed ±0.5%. We calculated mean density in g/cm^3 from the weight [mass] and volume of fresh bone. These parameters were determined without prior information about group classification of bone material. The obtained data were processed by methods of variation statistics.

Results and Discussion

In the weightless group of rats (FW)* there was 7.5% lag in weight gain of the tibia ($P>0.05$), as compared to the same parameter in animals from the synchronous experiment group (SW_1) (see Table).

Dynamics of weight, volume, mean density of fresh tibia and mineral content of its proximal epimetaphyseal region in different groups of experimental rats aboard the Cosmos-936 biosatellite (M±m)

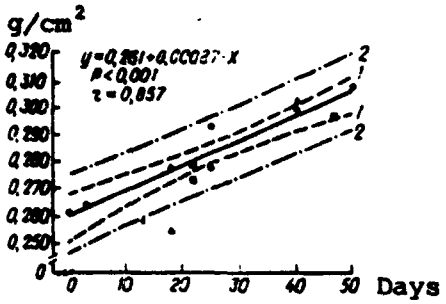
Phase of study	Group	Mass, mg	Volume, mm^3	Minerals, g/cm^2	Density, g/cm^3
Preflight	FW_1	391,8±9,5	277,5±4,4	0,262±0,004	1,412±0,023
	SW_1	415,3±9,1	292,5±6,1	0,265±0,003	1,420±0,005
Postflight	FW_1	439,5±14,6	312,0±11,3	0,255±0,005	1,410±0,009
	FC_1	464,8±7,2	325,5±6,2	0,278±0,005	1,429±0,009
	SW_1	475,6±8,5	326,8±5,6	0,273±0,003	1,455±0,008
	SC_1	474,0±4,0	323,0±2,7	0,278±0,004	1,462±0,007
	VC_1	537,6±15,6	363,0±9,7	0,294±0,007	1,481±0,006
	C_1^0	483,6±7,8	332,8±4,2	0,278±0,003	1,453±0,010
After 24-day recovery period	FW_2	562,8±12,3	376,6±7,5	0,302±0,004	1,494±0,004
	FC_2	582,6±15,0	381,8±10,0	0,299±0,003	1,526±0,010
	SW_3	553,6±15,8	360,0±11,5	0,296±0,007	1,538±0,006
	VC_2	536,4±13,5	349,8±8,2	0,308±0,003	1,533±0,004

The relative decrease in bone mass occurred with less marked decrease in bone volume (4%, $P>0.5$), which was indicative of development of osteoporosis. This was confirmed by data on mineral content of the proximal epimetaphyseal region and density of the whole bone. These parameters declined in the FW_1 group of animals (the differences were statistically reliable, as compared to values for animals in the SW_1 group). Since the density of whole bone is determined by the mineral content of the epimetaphyseal region, decrease thereof, as well as the general lag in increment of bone mass, are attributable chiefly to osteoporosis in the spongiform structures. The partial reduction of mass [weight] could be attributed to inhibition of bone growth, as indicated by the relative decrease in its volume. Consequently, two processes apparently affect the mechanism of development of osteoporosis: intensification of resorption and inhibition of osteogenesis.

Artificial gravity under weightless conditions prevents the above changes, as indicated by the fact that the tested parameters coincided with those of animals used in the synchronous experiment (FC_1 and SW_1 groups). This was indicative of the normalizing effect of 1 G accelerations on processes of physiological change in the bone in weightlessness.

The Table also shows that the tested parameters were virtually the same as in the control after a 25-day recovery period in the FW_1 group of rats, i.e., osteoporosis was reversible when the animals returned to earth.

*Translator's note: In animal group designations, F refers to flight group, W to weightlessness, S to synchronous experiment, C to use of centrifuge and VC to vivarium control.



Mineral content of proximal epimetaphyseal region of the rat tibia as a function of age in experiment aboard Cosmos-936.
Black circles--VC_1 group, white--C_1^0; white triangles--FW_1, black--FC_1; white squares--SW_1, dark--SC_1

1) range of 95% confidence interval for mean value of function in 11 animal groups, except FW_1 rats
2) range of 95% confidence interval for additional observation

It was difficult to assess the porosity of bones in each of the 12 groups because of differences in times at which the animals were sacrificed (see Table), since the density of spongiform bone structure (mineral content) is determined by age (see Figure). The mean group values shown in this figure for mineral content can be well approximated by a linear function of time in 11 groups, with the exception of the parameters for the FW_1 group of rats.

The regression analysis data illustrated in the Figure offer more validation for the conclusion that development of osteoporosis in rats during space flight is related to the effect of weightlessness, rather than the confined quarters in the satellite, and that artificial gravity prevents atrophic bone changes. The osteoporosis developing under the influence of weightlessness is apparently reversible.

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UDC: 629.78:612.452.018.015.36

STATE OF CATECHOLAMINES AND ENZYMES OF SYNTHESIS THEREOF IN THE ADRENAL MEDULLA OF RATS AFTER FLIGHT ABOARD COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 12 Aug 80) pp 64-65

[Article by R. Kvetnyanski, T. Torda, R. A. Tigranyan, Yu. Chulman and A. M. Genin]

[English abstract from source] In the adrenals of weightless and centrifuged rats flown for 18.5 days onboard the biosatellite Cosmos-936 indicators of the activity of the adrenomedullary system, i.e., the content of catecholamines and activity of the enzymes involved in their synthesis--tyrosine hydroxylase and dopamine-β-hydroxylase--were measured. It was found that none of the indicators changed postflight. These findings show that a prolonged exposure of rats to weightlessness does not act as a strong stressor for the adrenomedullary system.

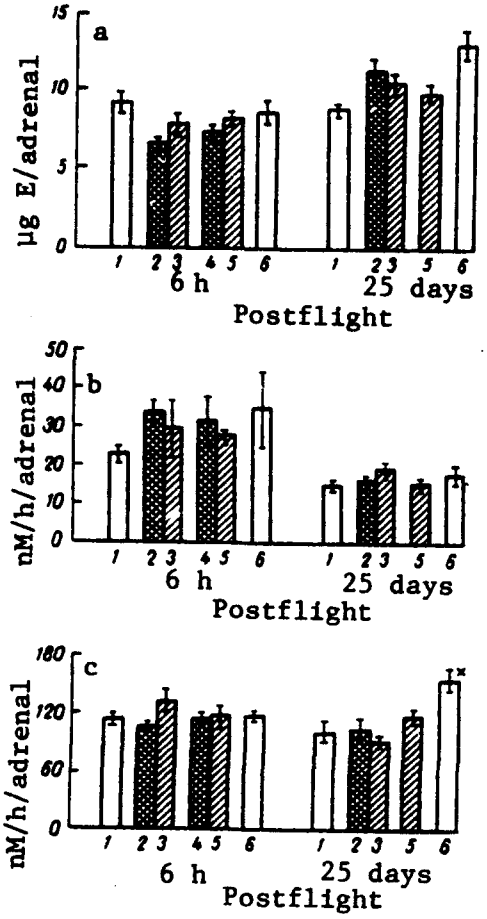
[Tebt] It has been demonstrated that epinephrine (E) content of rat adrenals diminishes under intensive and acute stress [1]. Chronic stress or daily exposure to an intensive stress factor elicits increase in activity of the rat's adrenal medulla, as manifested by increase in E and norepinephrine (NE) content, increased biosynthesis of catecholamines (CA) in the adrenals in vivo [2], particularly an increase in activity of enzymes of CA synthesis--tyrosine hydroxylase (TH), phenylethanolamine-N-methyltransferase [3] and dopamine-β-hydroxylase (DBH) [4].

Our objective here was to measure CA content and activity of enzymes of synthesis thereof in the rat adrenals after a flight aboard Cosmos 936 biosatellite, as well as to compare these data to the results of previous studies [5] and assess the duration of the effect of weightlessness on adrenomedullary function.

Methods

These studies were conducted on male Wistar-SPF rats (Bratislava, CSSR) flown for 18.5 days aboard Cosmos-936 biosatellite. The experimental conditions and designations of animal groups are described in [6].

We analyzed adrenals that were frozen in liquid nitrogen after the animals were decapitated. We determined CA content [7] and TH activity [8] in the left adrenal, and DBH activity in the right [9].



Levels (a), activity of TH (b) and DBH (c) in rat adrenals.
1-6) animals in VC, SW, FW, SC, FC and C^0 groups, respectively.
×) reliability as compared to vivarium control

Results and Discussion

There were no appreciable changes in E content or TG activity in the adrenals of rats used in space flight (FW [flight and weightlessness] and FC [flight and centrifuge] groups), as compared to animals in control groups SW [synchronous experiment, weightlessness], SC [synchronous experiment, centrifuge], VC [vivarium control] and C^0 [centrifuge], both 6 h and 25 days after landing (see Figure).

DBH activity of flight groups of rats also failed to change, as compared to animals in control groups SW, SC and VC. At the same time, we demonstrated significant increase in activity of this enzyme in control group C^0 when examined on the 25th day (see Figure), a finding that is difficult to explain.

The results obtained from the experiment conducted aboard the biosatellite Cosmos-782 revealed that there was no appreciable change in activity of the adrenal medulla in the course of a long-term space flight: a statistically reliable, although minor, increase in TH activity was found, which indicated that the rats had been under stress for a certain time [5]. It was not possible to determine whether this occurred under the influence of weightlessness or factors related to landing of the biosatellite, or else as a result of manipulations performed on the ground. In rats used in the experiment aboard Cosmos-936, TH activity, as a sensitive indicator of prolonged stress, did not change at all. This shows that no chronic stressogenic factor affected the animals during the 18.5-day space flight. This hypothesis is confirmed by the fact that adrenal TH activity increased by several times after exposure to chronic or recurrent stress [3, 10-13]. For example, repeated immobilization led to 3-4-fold increase in TG and DBH activity in rat adrenals [3, 4]. On the other hand, long-term exposure to weightlessness had no effect (Cosmos-936) or a minimal effect (Cosmos-782) on TG and DBH activity. It could have been assumed that activity of TH and DBH increases at the early stages of exposure to weightlessness, then TH activity gradually drops to the normal level. However, this is unlikely, since normalization of altered TH activity in rats occurred within about 2 weeks with the use of repeated immobilization [3] and exposure to cold [14].

CA content did not change appreciable, either in rats used in the Cosmos-782 experiment [5] or those in the Cosmos-936 experiment, which indicates that long-term weightlessness does not constitute intensive stress.

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UDC: 629.78:612.6-019:595.767.29

FLOUR BEETLE REPRODUCTION AND MUTABILITY IN WEIGHTLESSNESS (EXPERIMENTS ABOARD SALYUT-6 ORBITAL STATION)

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 16 Jun 80) pp 66-70

[Article by G. P. Parfenov]

[English abstract from source] Experiments with the flour beetle Tribolium castaneus showed that in weightlessness these insects completed their cycle of development--from fertilization to the emergence of mature imago of the next generation--in the normal way. Survival of specimens, densities of cultures, duration of development and frequency of morphoses in flight and control studies were similar. Exposure to weightlessness did not increase the number of genetic changes.

[Text] It is not by chance that experimenters are interested in the flour beetle as an object of investigation in the area of space biology. For several decades various species of beetles have been used in experiments, particularly in radiation and population genetics. Simple and precise methods of genetic analysis have been worked out for these insects, in particular, estimation of dominant lethals according to embryonic and larval deaths. An inexpensive nutrient medium, which is virtually not susceptible of being spoiled--flour, grain, bakery goods--is required for development of the beetles. The duration of beetle development from embryo to imago constitutes 40 days at 30°C. The density of beetle cultures at the embryo and young larva stages may reach several thousand per gram nutrient medium; for this reason, different experimental variants can be compared with statistical reliability. Finally, neither the nutrient medium nor the flour [or meal] beetle present any danger to man.

In 1967, the Tribolium confusum species of flour beetle was used by American specialists for an experiment aboard Biosatellite-2, the flight of which lasted 45 h [1]. The main objective of this experiment was to examine the nature of the combined effect of ionizing radiation and weightlessness on development and genetic processes. Some of the beetles had been exposed to γ-rays in a dosage of 1350 R prior to the flight. The fact of the matter is that the main parameter recorded--radiation-induced morphosis of the wings--is a distinct linear function of radiation dosage starting at about 2000 R [2], whereas the onboard source of γ-rays could only deliver a dose of about 1000 R. The beetles were at the pupal stage at the start of the experiment.

Weightlessness did not affect the parameters studied--survival, development time, wing morphosis and mutability. Inflight exposure to radiation decreased dominant lethals in females, as compared to the control., i.e., antagonism was demonstrable in the interaction of γ-rays and weightlessness. Conversely, in the case of 2-fold irradiation, the experimental females presented more dominant lethals. In addition there was an increased incidence of wing morphoses. Thus, we observed, it would seem, overt synergism of the effects of weightlessness and γ-rays. All these effects were on the borderline of statistical reliability (2.8% chance). The other parameters referable to the radiation part of the experiment did not differ statistically in the experiment and control.

We know of six publications concerning this experiment [1, 3-7]. In them, the authors interpret their findings differently, but they tend to believe that the effects, when considering dominant lethals, reflect distinctions of oogenesis and meiosis in female beetles, the latter being very irregular in time and its stages are characterized by differences in radiosensitivity. Embryos that developed from germ cells that were at different stages during exposure to radiation may have been submitted to analysis in the different experimental variants.

The difference in upkeep temperature for experimental and control beetles could elicit an increase in incidence of wing morphoses. A temperature of 32°C is the optimum for beetle development. Deviations of 8-10°C from the optimum (in either direction) elicit approximately 10% increase in incidence of morphoses [8]. Moreover, it has been established that temperature and ionizing radiation have a synergistic effect on appearance of these anomalies [9].

Tr. castaneum was the flour beetle species used in the experiment aboard Cosmos-605 biosatellite [10]. The results of experiments conducted with Tr. confusum and castaneum are entirely comparable. These species have similar ecology. The size of specimens and time of development are virtually the same. Species-specific differences related to the structure of antennae and distance between eyes are the most noticeable and convenient to identify. The studies with beetles aboard Cosmos-605 biosatellite were embryologically oriented. Since there was not enough time for the complete cycle of development of beetles during this flight, which lasted about 20 days, the specimens placed on board were at the embryo, larva and pupa stages. It was established that weightlessness does not create difficulties in hatching of larvae, pupation or metamorphosis. The survival rate of the specimens at all stages of development was about the same as in the control.

With respect to dominant lethals, a statistically reliable increase in incidence was demonstrated in one experimental variant out of six, namely in the gametes of females that developed from specimens placed on board at the embryo stage.

Wolfgang Briegleb et al. conducted a large cycle of studies using both Tr. confusum and castaneum flour beetle species in clinostats [11-14]. One of these experiments lasted 20 months. In this time, there were eight generations of beetles. It was concluded from the cycle of studies that exposure to conditions simulating the effect of weightlessness for many months had no appreciable effect on duration and morphological parameters of development, and did not elicit genetic changes. The authors called attention to the fact that, when interpreting the experiments with this beetle, one should be particularly cautious, since this species has a special mechanism for controlling population size. A chemical substance, kuinin, is secreted by beetles in overpopulated cultures, which lowers fertility and can elicit a teratogenic effect. In addition, cannibalism is observed in overpopulated cultures--imagos may consume the eggs.

Various physical factors, including temperature and composition of the atmosphere, as well as magnetic fields, may affect development and mutability of flour beetles [15]. Each factor has its own range, within which the normal reaction occurs. In the cited report, the author did not rule out the possibility that weightlessness and ionizing radiation could have synergistic action, eliciting anomalous development and mutations.

Flour beetles as, apparently, all insects are extremely resistant to hypergravity.

The duration of the flight aboard the Salyut-6 orbital station made it possible to investigate the morphology and mutability of the flour beetle at the time the cycle of its development began and ended in weightlessness. This is the main distinction of this study, as compared to the preceding ones. Participation of the cosmonauts in this study assured reliable performance of the operations to cross specimens and move them to fresh nutrient media.

Methods

We used a normal strain of Tr. castaneum isolated from a wild population near Moscow in 1970 and maintained in the laboratory by means of mass scale crosses on standard nutrient medium (94% wheat flour and 6% dry brewer's yeast). This strain was notable for good fertility and relatively low level of spontaneous anomalies in wing structure (about 2%).

Four experiments were conducted with the beetles aboard the Salyut-6 orbital station: two during the first main expedition and two during the second main expedition (Table 1).

Table 1. Main data concerning the experiment

Parameter	Expedition			
	first		second	
	experiment			
	1	2	1	2
Purpose of experiment	Reproduction	Mutability	Reproduction	Mutability
Weightlessness, days	39	39	80	21
Stage of development at start of experiment	Imago	Larva	Pupa	Eggs and larvae
Number of specimens at start of experiment	10 pairs	200	10 pairs	100 eggs, 100 larvae

For all of the experiments we used SMO (system for multicellular organisms) instruments, which were installed aboard Soyuz spacecraft and after docking with the Salyut-station transferred to the latter and placed in temperature-controlling devices. The latter equipment operated at 30°C. The SMO instrument is a parallelepiped 82×62×57 mm in size, divided into four inside sections. Each section had a removable feeder, into which the experimental specimens and nutrient medium were placed. There were levers to connect or disconnect adjacent sections in the top part of the instrument.

The operations performed by the cosmonauts consisted of raising and dropping the gates connecting different compartments of the instruments, by means of the levers. In the experiments dealing with the study of development, at the start of the missions the gates were opened for 1 day so that the males and females could mate. In the experiments dealing with mutability, the gates were opened to transfer some of the beetles to adjacent compartments with fresh nutrient medium at the time when, according to estimates, the developmental cycle was terminated, and the specimens placed on board at the embryo and larva stages reached the imago stage.

After returning the instruments to the laboratory, in the experiments dealing with development we counted the live and dead specimens at all stages of the life cycle. Then the imagos, as well as larvae and pupae as they changed into imagos, were tested for wing morphoses. Specimens at the egg stage were not tested for this character, since it was assumed that many eggs were laid after landing.

According to external signs, sexual dimorphism was distinctly manifested in these beetles only at the pupal stages [16]; for this reason, the experiments dealing with mutability of crosses were conducted with specimens that were at the larval and pupal stages after landing. As they underwent pupation, the specimens were divided into males and females. Imagos were crossed at the age of 8-10 days. Consequently, gametes that had been at the early stages of development in flight were submitted to analysis. It was considered that all eggs that did not produce larvae had a dominant lethal. For this reason, the demonstrated incidence of lethals was overstated, since unfertilized eggs fell into this category. Experimental and control imagos were crossed with individuals of the opposite sex selected from laboratory cultures.

Results and Discussion

Table 2 lists data on beetle reproduction. In experiment No 1, in both the experiment and the control, live and dead imagos were the parents. The short duration of the experiment (39 days) did not permit complete development. But in experiment No 3, there were more live imagos than parents. In this experiment, the imagos were apparently represented by both parents and first-generation specimens, which were conceived and underwent the full cycle of development in weightlessness. In most cases, the dead imagos were referable to the parental generation.

Table 2. Reproduction of flour beetle in weightlessness. Number of specimens demonstrated after landing, at different stages of development

Exper. No	Variant	Stage of development				Morphoses	
		imago	pupa	larva	egg	absol.	%
1	Experiment	12 (8)	71	84	2115 (150)	5	2.9
	Control	18 (2)	105	81	2470 (235)	5	2.5
3	Experiment	62 (17)	18	35	8784 (377)	4	4.9
	Control	30 (24)	16	43	10 333 (550)	4	4.4

Note: Number of dead specimens is given in parentheses.

The data in Table 2 show that, in both experiments (No 1 and No 3), experimental and control beetle cultures resembled one another in number of specimens and incidence of wing morphoses. In all variants, we were impressed by the dissimilar

number of specimens at different developmental stages. The number of specimens should be proportionate to the duration of a stage. In actuality, there were considerably more embryos (eggs). Apparently, the mechanism of population control by means of cannibalism came into play. The imagos consumed embryos and young larvae intensively; for this reason a relatively small number reaches the stages of advanced larvae and pupae. The increase in incidence of morphoses in experimental and control cultures in experiment No 3, as compared to No 1, is perhaps attributable to accumulation of the teratogenic effect of kuinin. Experiment No 3 lasted considerably longer.

Table 3.
Mutability of flour beetle in weightlessness. Appearance of dominant lethals in gametes of males and females

Exper. No	Sex	Variant	Parents	Deposited eggs	Hatched larvae	Lethals	
						abs.	%
2	F	Exper.	5i	748	678	70	9.4±1.1
		Control	71	1241	1115	126	10.2±0.8
	M	Exper.	12	788	742	46	5.8±0.8
		Control	50	854	820	34	4.3±0.7
4	F	Exper.	84	1215	980	235	19.3±1.1*
		Control	80	1010	869	141	14.0±1.1
	M	Exper.	122	2218	1970	248	10.9±0.7
		Control	177	2111	2190	221	9.2±0.6

* $P < 0.01$.

Table 3 lists data on genetic changes in beetle gametes expressed as dominant lethals at the embryonic stage. The dominant lethals were induced by chromosomal aberrations associated with major deficiencies and aneuploidy--shortage of an entire chromosome [17]. Unfertilized eggs are usually included with dominant lethals. From the genetic point of view, they can be interpreted as a shortage of half the genome, but of course their appearance is unrelated to the effect of germ cells on nuclei. Unfertilized eggs and those with dominant lethals differed in time of death. Mitotic divisions did not start and blastulas did not form in the former, while the latter usually perished at various stages after formation of the blastula. However, in setting up mass scale experiments, major errors can be made in determining the causes of egg death, since the early stages of embryonic development are very rapid. The blastula is formed 4 h after fertilization.

Statistically, the incidence of dominant lethals in experimental and control series was the same in three out of four variants. In one variant, the incidence of dominant lethals in gametes of females in experiment No 4 was higher, with statistical reliability, than in the control. Interestingly enough, in all variants, the incidence of lethals was higher in female gametes, both in the experiment and the control. In laboratory cultures, when determining the spontaneous incidence of dominant lethals, they should and do occur in the same number in males and females. The higher incidence of lethals in experimental and control females in the experiments aboard the Salyut-6 orbital station unquestionably reflects a decline of capacity for fertilization, decrease in fertility, i.e., the effect of transfer into the SMO instruments.

Of course, the statistically reliable increase in dominant lethals among females in experiment No 4 should not be related to the effects of weightlessness. The data from the other three variants and all of the results obtained in previous experiments with flour beetles are in contradiction with this. Most likely, the experimental SMO instrument was exposed to unfavorable temperatures at the final stages of the experiment, and they were instrumental in lowering fertility of females.

The results of these experiments revealed that beetles undergo the entire developmental cycle in weightlessness, from fertilization to appearance of puberal specimens of the next generation. Only a qualitative assessment can be made of the survival rate; apparently it was not lower than in the control. It is not deemed possible to differentiate between the effects of physical upkeep conditions on number of specimens from biological regulation thereof because of the high density of cultures that we demonstrated, which were probably at a maximum.

Similarly, we can only offer a qualitative evaluation of development time. Serious analysis of changes in this parameter is meaningless, since duration thereof depends strongly on temperature. For example, at 20°C, the pupal stage lasts 24 days and at 30°C only 6 days, and the temperature levels did not coincide exactly at the start and end of the experiment. Nevertheless, the obtained data enable us to maintain that beetles developed in weightlessness without any appreciable disturbances, and both survival rate and duration of development were close to normal.

An equally definite conclusion can be derived on the basis of the results obtained in the tests for mutability: weightlessness did not elicit genetic changes in either male or female gametes. More precisely, weightlessness did not induce genetic changes interpreted as dominant lethals.

Development of three insect species was studied in weightlessness: the Drosophila, Habrobrason flies and the flour beetle. In all cases, the results were analogous: no changes were demonstrated in speed and nature of development. There are probably sufficient grounds to assume that, with the meroblastic type of cleavage of ovicells inherent in insects, changes in gravity in either direction do not affect development so long as the mechanical integrity of the embryo is preserved. The results of the genetic tests with the flour beetle confirm the view that weightlessness is not (at least not for the positive objects we studied) an active mutagenic factor.

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COMPUTER USE FOR AUTOMATIC MEASUREMENT OF SOME PHYSIOLOGICAL PARAMETERS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 24 Sep 80) pp 70-73

[Article by V. A. Degtyarev, N. M. Zhurba, Yu. A. Kukushkin, V. G. Doroshev and N. A. Lapshina]

[Text] Questions of assessing and forecasting the condition of cosmonauts aboard manned orbital stations (MOS) are of exceptional importance [1, 2]. To answer them, ongoing measurements must be taken of physiological parameters that are recorded in the course of medical monitoring of MOS crews. It is expedient to implement this process by means of computers.

Our objective here was to explore the possibility of automatic processing of some hemodynamic parameters included in the set of medical monitoring methods for MOS crews.

Methods

We recorded synchronously the physiological parameters of sphygmograms of the carotid, radial and femoral arteries (SPG_c, SPG_r, SPG_f), kinetocardiograms (KKG), tachooscillograms (TO) and electrocardiograms (EKG) with an onboard Polynome-2M apparatus, then interpreted these curves automatically and calculated the hemodynamic parameters with a computer.

The process of obtaining hemodynamic parameters with a computer consists of two stages: interpretation of physiological curves, which consists of finding typical points on the curves and measurement of time and amplitude intervals between them; calculation of hemodynamic parameters using certain formulas, which include data obtained at the first stage, and output of the results on an alphanumeric printing device and display. The developed algorithms for interpretation of physiological parameters are based on principles that simulate the actions of a physician when interpreting them manually, for which purpose the knowhow and experience of medical workers in this direction were used. The interpretation algorithms consist of logical rules for determining certain points on physiological curves within specified time intervals. The choice of duration of these intervals is made either in fractions of RR on the EKG, or on the basis of estimation of physiologically permissible range of a given process during function of the human cardiovascular system.

We determined on the SPG_c, SPG_r and SPG_f curves the starting point of the pulse wave in order to calculate the rate of propagation thereof over arteries of the elastic and muscular type, and the incisura point on the SPG_c curve to calculate the period of ejection of blood.

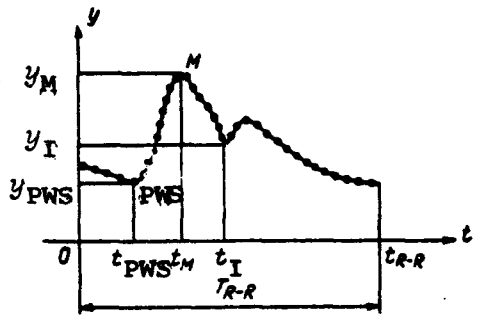

Figure 1.
Cardiac cycle on sphygmogram of the carotid

We found points 2, 3, 4, 7 [3] on the KKG curve recorded synchronously with the EKG in order to calculate the phases of asynchronous and isometric contraction, and the ejection period.

We found points on the TO curve corresponding to minimum, mean dynamic, lateral and end systolic arterial pressure [4].

The algorithms for calculation of hemodynamic parameters consist of a number of formulas taken from [3-5], with which the arterial pressure, phase structure of the cardiac cycle, cardiac function and peripheral resistance were calculated. We compared the effectiveness of the algorithms for interpretation of SPG_c, SPG_r, SPG_f, KKG, TO and EKG to the results obtained with the computer and by physicians using manual decoding.

Results and Discussion

To interpret physiological curves with a computer using the developed algorithms, first the physiological data are processed in order to reduce the number of random errors and interference, which occur as a result of coding analog information and inputting it in the computer, as well as to break the curves down into cycles of a specific duration.

The obtained data are smoothed to reduce random errors and interference by the least squares method, using a first degree polynome for three points:

$$\overline{f}_i = \frac{1}{3}(f_{i-1} + f_i + f_{i+1}) \qquad (1)$$

where fi is the smoothed value of the ith point on a discrete curve; fi_{-1}, fi and fi_{+1} are the base values for the discrete curve.

Use of sliding mean filter (1) has virtually no effect on accuracy of determination of characteristic points.

When marking the curves into cycles, consideration is given to the location of the R wave of the EKG. Marking consists of determining reference points on the curves, from which starts interpretation of each cycle of the corresponding curve. The algorithm for determining the R wave of the EKG with a computer has been described previously [6].

In this report, we describe the algorithm for interpretation of the SPG_c curve as an example. To describe the algorithm for finding characteristic points on the sphygmogram of the carotid artery, the SPG_c curve is represented by a flat curve,

$y = f(t)$, which is discretely specified in the interval of T_{R-R} which equals the duration of cardiac cycle R-R on the EKG. An example of an analyzed cycle on the SPG_c curve is illustrated in Figure 1.

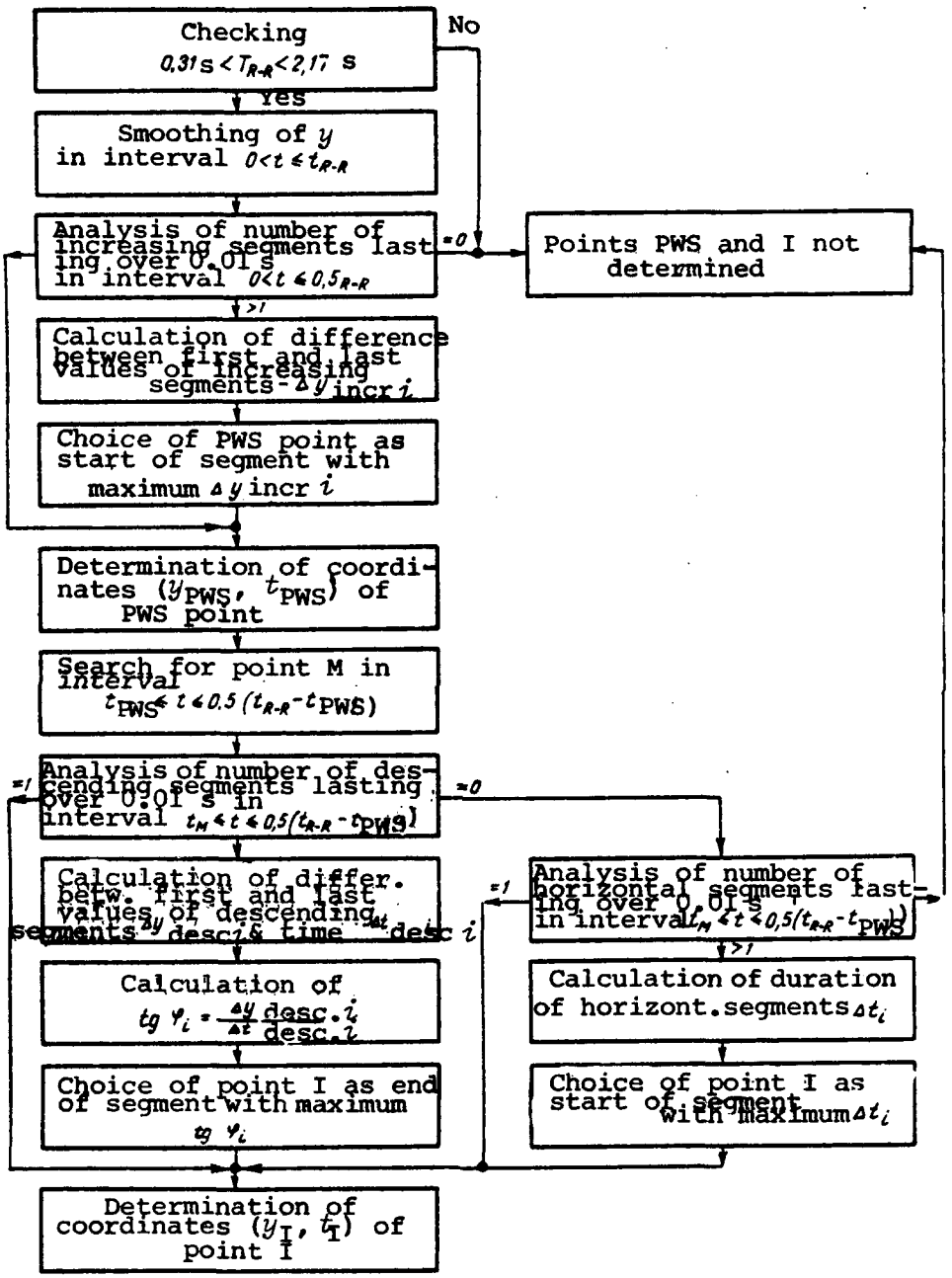

Figure 2. Flowchart of algorithm. Explanation is given in the text.

The algorithm for determining the starting points of the pulse wave (PWS) and incisura (I) consists of the following.

1. Checking duration of T_{R-R} interval for conformity with the condition:

$$0.31 \text{ s} < T < 2.17 \text{ s}$$

If this condition is not satisfied, the starting points of cycles are not determined.

2. Smoothing of y in the interval of $0<t\leqslant t_{R-R}$ with a first degree polynome for three points.

3. Calculation of differences $\Delta y_i = y_{i+1} - y_i$ in the interval $0<t\leqslant 0.5\ t_{R-R}$.

4. Selection of increasing [or ascending] segments of y lasting over 0.01 s in the interval of $0<t\leqslant 0.5\ t_{R-R}$.

5. Analysis of y according to number of increasing segments.

If there is only one such segment, the start of this segment is taken as the PWS point; then one should move to step 9. If there are more than one segment, one should go on to step 6. If there are no increasing segments, the PWS point is not determined and one should go on to step 10.

6. Calculation of differences between first and last values of increasing segments $\Delta y_{\text{incr}.i}$.

7. Search for maximum value of $\Delta y_{\text{incr}\,i} - \Delta I$.

8. Analysis of number of ΔI. If there is only one such value, the starting point of this ascending segment is taken as the PWS point. If there are more than one such value, the PWS point is not determined and one should proceed to step 10.

9. Storing coordinates (y_{PWS}, t_{PWS}) of the PWS point. Then one should go to step 11, which is the start of searching for point I.

10. Reporting impossibility of determining the PWS point in this cycle of the curve, then one should go to step 19.

11. Search for maximum (M) point on curve y in the interval of $t_{PWS}<t\leqslant 0.5\ (t_{R-R} - t_{PWS})$.

12. Calculation of differences $\Delta y_i = y_{i+1} - y_i$ in the interval of $t_M<t\leqslant 0.5\ (t_{R-R} - t_{PWS})$.

13. Selection of descending [decreasing] y segments lasting over 0.01 s in the interval of $t_M<t\leqslant 0.5\ (t_{R-R}-t_{PWS})$

14. Analysis of y according to number of descending segments. If there is only one such segment, the end point of this segment is taken as point I, and then one proceeds to step 18. If there are more than one such segment, one should go to step 15. If there are no descending segments, one should proceed to step 20.

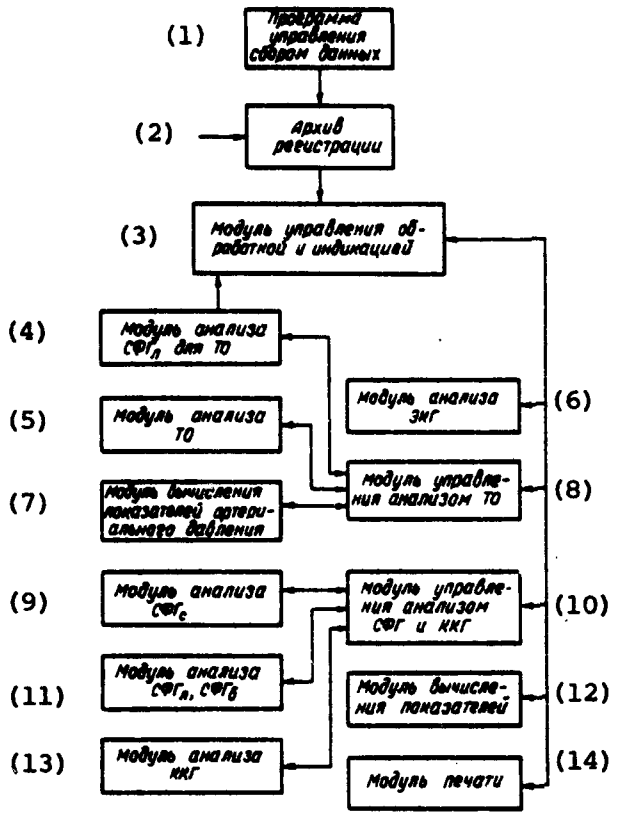

Figure 3.
Package structure

Key:
1) data gathering control program
2) record file
3) modulus for control of processing and display
4) modulus of analysis of SPG_r for TO
5) modulus for TO analysis
6) modulus for EKG analysis
7) modulus for calculation of arterial pressure parameters
8) modulus for control of TO analysis
9) modulus for SPG_c analysis
10) modulus for control of SPG and KKG analysis
11) modulus for SPG_r and SPG_f analysis
12) modulus for calculation of parameters
13) modulus for KKG analysis
14) modulus for printout

15. Calculation of differences between first and last values of descending segments $\Delta y_{\text{desc.}i}$ and duration of these segments $\Delta t_{\text{desc.}i}$.

16. Calculation of values of $\text{tg}\phi_i = \frac{y_{\text{desc.}i}}{t_{\text{desc.}i}}$.

17. Choice of maximum value $\text{tg}\phi_{\max}$ and determination of point I as the end point of this descending segment, then go to step 18. If such a value is not selected unequivocally, point I is not determined and one should proceed to step 19.

18. Storing coordinates (yI, tI) of point I.

19. Reporting impossibility of finding point I on the curve.

20. Selection of horizontal segments of y lasting over 0.01 s in the interval of $t_M \leqslant t \leqslant 0.5\ (t_{R-R} - t_{PWS})$.

21. Analysis of y according to number of horizontal segments. If there is only one such segment, its start is taken as point I; then one should go to step 18. If there are more than one such segment, one should move to step 22.

If there are no horizontal segments, point I is not determined and one should move to step 19.

22. Determination of duration of horizontal segments Δt_i.

23. Search for maximum value of $\Delta t_i - \Delta T$.

24. Analysis of y according to number of ΔT with maximum value. If there is only one such value, the start of this horizontal segment is taken as point I, then one should go to step 18. If there are more than one value, point I is not determined and one should move to step 19.

Figure 2 illustrates the flowchart of the algorithm for determining PWS and I points.

The algorithm for finding the PWS point on the SPG_r and SPG_f is analogous to the one used to find the PWS point on the SPG_c.

The programmed execution of algorithms for interpretation of hemodynamic parameters is in the form of a package of applied programs for computers. The programs contained in the package are constructed as separate moduli, which function either independently or under the control of control moduli. The structure of the package is illustrated in Figure 3.

A physician usually spends 3-3.5 h per test to interpret and obtain derivative circulatory parameters. Use of a computer for this purpose reduces time by 50-60 times.

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METHOD FOR EVALUATING RESPIRATORY SYSTEM REACTION TO INCREASING HYPERCAPNIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 10 Jul 80) pp 74-76

[Article by L. A. Ivanov]

[Text] The potential possibility of hypercapnia during space flights makes it imperative to pursue in-depth studies of the effects of CO_2 on different aspects of vital functions. Our objective here was to examine the effects of increasing hypercapnia on ventilatory function of the lungs.

Methods

We examined 18 essentially healthy men 18-29 years of age. We used the method of R. S. Vinitskaya and N. A. Koganova [1] to test the effect of progressive hypercapnia on pulmonary ventilation. According to this method, the subject breathes from a spirograph, from which the CO_2 absorber was removed. A carbograph is connected in parallel with the spirograph in order to record CO_2 concentration concurrently with pulmonary ventilation. One finds the points in the system of coordinates characterizing the correlation between partial CO_2 tension in alveolar air and tidal volume by plotting the former (p_ACO_2) on the x-axis and the corresponding V_T on the y-axis. By drawing a line through these points, one obtains a curve of tidal volume as a function of p_ACO_2, which reflects the reaction of the respiratory center to CO_2. The intersection of this line on the x-axis corresponds to the point that characterizes p_ACO_2 level, at which ventilation equals zero. This is the so-called apnea point, which reflects sensitivity of the respiratory center to CO_2.

In this work, the method for conducting the investigation was used with the following modifications.

1. In view of the fact that not only tidal volume, but respiration rate [2, 3], change in the presence of hypercapnia, p_ACO_2 level was not compared to tidal volume, but to minute volume of respiration (MV).

2. A Fleisch head--pneumotachograph sensor--was placed between the mouthpiece and front valve of the spirograph. A Godart two-channel pneumotachograph automatic printer was used for continuous recording of integral respiration rate and MV. As a result, it was possible to record the recovery period of pulmonary ventilation after hypercapnia.

3. The study was pursued until the subject refused to breath from the spirograph. This enabled us to determine resistance to hypercapnia and determine the functional capacity of the respiratory center in the presence of increasing CO_2 concentrations.

During the hypercapnic test, O_2 content of the working system of the spirograph was monitored with an MMG-7 oxygen analyzer.

Upon reaching the maximum pulmonary ventilation at the end of the hypercapnic tes we collected arterialized capillary blood to determine the parameters of acid-base balance and PO_2. To arterialize blood, the fourth finger, from which blood was taken, was submerged for 10 min in water at a temperature of 45-50°C. The tests were conducted on an RNM-71 type micro-Astrup apparatus.

Results and Discussion

As shown by the results of the studies, the test was stopped when p_ACO_2 constituted 65.2±1.45 mm Hg, a parameter which we designated as the maximum p_ACO_2. The test was usually discontinued at the request of the subject due to unpleasant dyspnea, less often due to vertigo, headache and febrile feeling. We failed to observe any side-effects that would present a hazard. Indeed, according to data in the literature, side-effects of CO_2, in particular, psychoneurological symptoms, start to appear only with p_ACO_2 of the order of 80-90 mm Hg [4], i.e., with a considerably higher level of hypercapnia.

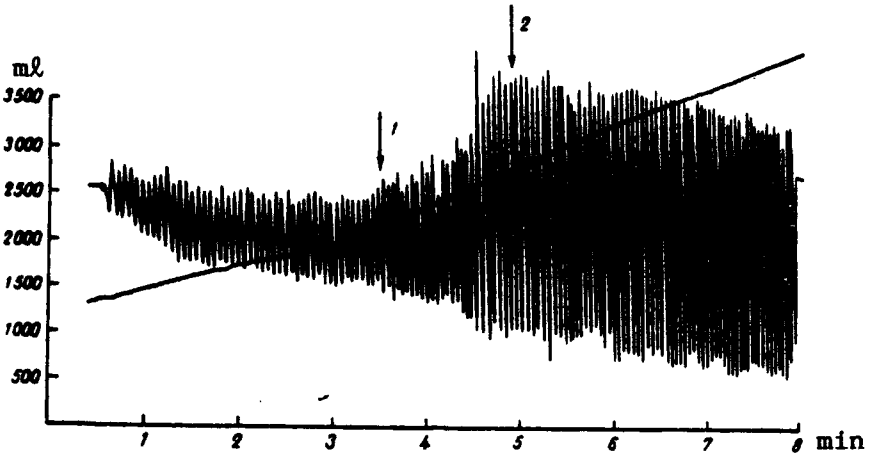
The changes in blood pH at peak hypercapnia were characterized by development of decompensated gas acidosis (pH dropped from 7.407±0.024 to 7.322±0.016; $P<0.05$). In addition, there was elevation of true plasma bicarbonate level (from 25.7±0.6 meq/ℓ to 28±0.3 meq/ℓ; $P<0.05$), which is attributable to the increase in concentration of blood carbonic acid in the presence of hypercapnia, which is dissociated into ions of hydrogen and bicarbonate. The hydrogen ion combines with buffer bases (mainly protein and phosphate ones) and is eliminated, while the bicarbonate ion remains in plasma, causing retention of the sum of positive and negative charges in the system.

We observed elevation of P_aO_2 (from 74.9±1.25 mm Hg to 81.6±1.6 mm Hg; $P<0.05$) under hypercapnic conditions, which conforms to the findings of V. V. Zhuravlev [5]. It should be noted that the O_2 concentration in the closed system of the spirograph underwent virtually no change during the test, since the design of the spirograph (tank with O_2 supply, automatic system for stabilizing oxygen) provides for replenishing O_2 consumed from the working system of the instrument. For this reason, it must be assumed that the elevation of p_aO_2 during the hypercapnic test was attributable to CO_2-induced hyperventilation.

Examination of the reaction to hypercapnia, which lasted until the subject refused to continue with the test, helped us demonstrate the phenomenon of a three-phase ventilation reaction to CO_2 (see Figure).

The phasic ventilation reaction to hypercapnia consisted of the fact that MV increased gradually and mildly at the first stage of the test (first phase) then did so faster and more severely (second phase). The MV increment scaled to 1 mm Hg elevation of p_ACO_2 constituted 878±89 mℓ in the first phase and 1662±184 mℓ in the second. At the end of the test, ventilation reached a stable level and did

not increase further, in spite of the continuing rise of p_ACO_2 (third phase). The first phase lasted 111.9±10.4 s, the second 210.4±22.5 and the third 117.3±13.2 s, with total duration of the hypercapnic test of 434±33.7 s.



Spirogram of subject D. during hypercapnic test

1) change from first phase of change in ventilation to second with hypercapnia
2) change from second phase of change in ventilation to third

We demonstrated distinct qualitative differences in ventilation dynamics in the presence of hypercapnia as a function of phase of reaction. During the first phase, respiration rate decreased by 2.5±0.8 ($P<0.01$), as compared to the base level, i.e., the increase in ventilation was attributable entirely to tidal volume. This is consistent with data concerning reciprocal correlations in the dynamics of tidal volume and respiration rate in the presence of hypercapnia [6]. Respiration rate increased appreciably (by 3.9±9; $P<0.003$) only in the second phase. This slower increase in respiration rate, as compared to tidal volume, in the presence of hypercapnia had been reported also by Reynolds et al. [7]. However, the increment of respiratory rate in the second phase was also considerably smaller than the increase in MV. Thus, at the end of the test, MV showed approximately 5-fold increase, as compared to base level, whereas respiration rate increased by only 1.3 times, i.e., even in the second phase ventilation increased chiefly at the expense of tidal volume.

With reference to the mechanism of this phasic reaction, we can expound the following hypothesis. As we know, CO_2 affects the pulmonary reaction in two ways: a) stimulation of chemoreceptors of the aortic and particularly sinocarotid zone [8]; b) direct stimulation of chemoreceptors of the brain stem reticular formation [9]. We demonstrated some specificity to the role of these two mechanisms in regulating respiration in the presence of hypercapnia. Arterial chemoreceptors are responsible for the first, rapid phase of the ventilatory reaction to CO_2. At the same time, central regulatory mechanisms play a quantitatively larger part in the ventilation reaction to prolonged hypercapnia. Thus, the 60-80% increase in ventilation during hypercapnia could be attributed to stimulation of central chemosensitive structures by virtue of their greater reactivity to CO_2 and acidosis [10].

On this basis, it may be assumed that peripheral chemoreceptors play a large part in intensifying ventilation at the early stage of exposure to CO_2. Then, as hypercapnia increases, there is an increase in the role of the direct effect of high CO_2 level on chemoreceptors of the respiratory center. The subsequent increase in role of the centrogenic effect of hypercapnia is manifested by the drastic increase in ventilation (second phase).

This hypothesis was confirmed when we examined the value of p_aCO_2 corresponding to the change from the first phase of the ventilation reaction to the second, which we designated as transient p_ACO_2. The transient p_ACO_2 constituted 51.3±1.35 mm Hg, and was found to be higher than pCO_2 of venous blood with normocapnia. This fact means that, as the first phase of hypercapnic increase in ventilation progresses into the second phase, there is significant elevation of pCO_2 of tissues, including the respiratory center. In this regard, we were impressed by appearance of the awakening effect of CO_2 on dogs, which is indicative of the marked influence of hypercapnia on central regulatory structures when p_ACO_2 is somewhat higher than $pVCO_2$ [11].

As for the third phase of the ventilation reaction to hypercapnia, the MV level at this time (which we designated as maximum MV) constituted 40.3±2.36 ℓ. This parameter was about 3 times smaller than maximum pulmonary ventilation (122±6.2 ℓ) previously obtained for a group of subjects analogous in age, sex and health status [12]. For this reason, it can be assumed that maximum MV in the presence of hypercapnia is limited by the functional capabilities of the respiratory center, which regulates pulmonary ventilation, to a greater extent than by those of pulmonary ventilation itself. The p_ACO_2 level, at which no further increase in ventilation was observed (which we designated as threshold p_ACO_2; 61.2±1.1 mm Hg), was reliably lower than the maximum level. Apparently, the threshold p_ACO_2 characterizes the level of hypercapnia, at which impulsation from the respiratory center reaches a maximum, while maximum MV reflects the intensity of impulsation from the respiratory center, which stimulates pulmonary ventilation.

Because of the phasic nature of the ventilation reaction to hypercapnia, one should plot the curve of ventilation as a function of p_ACO_2 by the method of R. S. Vinitskaya and N. A. Koganova in accordance with the first phase of the ventilation reaction. In this case, it is possible to compare the results of the study to data of other authors who used the same method and characterize sensitivity to hypercapnia of expressly peripheral chemoreceptor structures.

The angle of inclination of the line of MV as a function of p_ACO_2, which reflects the reaction of ventilation to hypercapnia, constituted 60.4±1.39°, which is close to the data of R. S. Vinitskaya and N. A. Koganova [1]. The apnea point constituted 27.7±1.43 mm Hg, and corresponded to indications that stimulation of receptors by hypercapnia begins with p_ACO_2 of the order of 20-30 mm Hg [13].

It is of considerable interest to examine the period of recovery of pulmonary ventilation after hypercapnia. The p_ACO_2 level was restored 56.4±11.2 s after termination of the test. For this reason, it can be maintained that posthypercapnia stabilization of MV, which requires 5 times more time (257.5±221 s) than restoration of p_ACO_2 level, characterizes the duration of the excitatory process in the respiratory center, which was induced by hypercapnia. In view of the fact that stabilization of MV after hypercapnia depends, to some extent, on ventilation level at the end of the test, one can offer a more accurate description of the

period of recovery of ventilation after hypercapnia by relating the MV decline to duration of the decline and calculate the rate of recovery of MV. In this case, it constituted 125.6±11.63 mℓ/s.

Thus, with progressive hypercapnia leading to development of decompensated gas acidosis and associated with elevation of p_AO_2, there is an increase in pulmonary ventilation proportionate to the increase in p_ACO_2. The reaction of ventilation to hypercapnia occurs in three phases, with more marked increase of MV in the second phase and a stable MV level in the third phase. Several parameters have been proposed (maximum p_ACO_2, maximum MV, threshold p_ACO_2, transient p_ACO_2), which characterize the distinctions of the body's reaction to hypercapnia. The duration of restoration of MV level after hypercapnia is largely determined by the speed of regression of the excitatory process in the respiratory center, which had been elicited by hypercapnia.

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LOG-LINEAR REGRESSION METHOD USED TO ASSESS QUALITY OF AIR SAMPLES IN FLUOROPLASTIC CONTAINERS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 17 Mar 80) pp 76-78

[Article by V. Ye. Ryzhkova, Ye. N. Kul'kov and K. N. Mikos]

[Text] Collection and storage of samples play a rather important part in performing chemical analysis of air mixtures or gases. Special attention is being given to this matter, since there can be partial loss of substances to be analyzed in the course of storage thereof [1].

Methods

We used soft containers with 5-7-ℓ capacity, made of fluoroplastic to collect air samples. The containers consisted of two-ply [double layer] film, cover and metal plate with an opening to deliver and remove air. There were a clamp and plug on vacuum hoses connected hermetically to the openings in the metal plate to assure a tight seal of the container. Figure 1 shows the general appearance of the containers. Before use, the containers were flushed many times with extra-pure helium and vacuumed.

We tested the possibility of using these containers for storage of air samples containing traces of organic matter, using artificial air mixtures. We tested the quality of the gas samples in the containers for 10 days, using mixtures differing in concentration. Gas chromatographic analysis of samples from the containers was performed immediately after they were filled with a mixture, after 4, 6, 8 and 24 h on the first day, then once a day.

Analysis of the air mixture was performed on a chromatograph with ionization-flame detector. The air mixture was separated in a steel column 1.5 m in length, which was filled with poropak [?] Q (column temperature 150°C; after filling, temperature in the column was held at 135°C and injector temperature 150°C). It was sufficient to take samples of 1 mℓ air to perform such analysis.

Results and Discussion

Figures 2 and 3 illustrate the curves of changes in concentration of methane, ethane, methanol, ethanol, acetone and ethyl acetate as a function of time. As can be seen in Figures 2 and 3, there was virtually no change in concentrations of saturated hydrocarbons (methane, ethane) during storage. There was exponential

change in levels of oxygen-containing organic substances (methanol, ethanol, acetone and ethyl acetate). The change was particularly intensive in the first 6 h, after which the process slowed down. The nonlinear nature of decrease in concentrations was apparently related to two processes: adsorption of substance on the inside surfaces and diffusion through the walls. However, adsorption probably plays the leading role, particular if we are dealing with storage of such markedly polar organic substances as methanol, ethanol, acetone and ethyl acetate. The dipole moment is 1.7 for methanol, 1.68 for ethanol, 2.85 for acetone and 1.81 for ethyl acetate; there are no dipole moments for methane and ethane, i.e., they equal zero. Regression analysis was performed to demonstrate dependence of concentration of substances on storage time. In view of the nonlinearity of the process, the data are submitted in logarithmic form.

Figure 1. General view of container

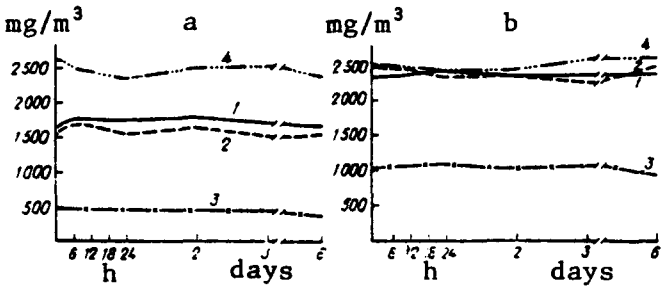

Figure 2. Change in concentration (a) and ethane (b) during storage in fluoroplastic containers.

Here and in Figure 2: 1-4) containers No 1-4, respectively

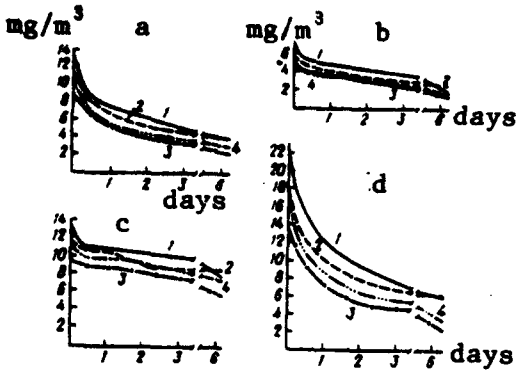

Figure 3.
Curves of change in concentrations of acetone (a), methanol (b), ethanol (c) and ethyl acetate (d) stored in fluoroplastic containers

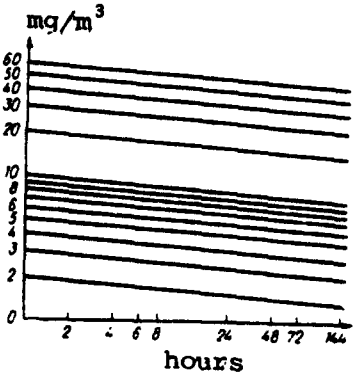

Figure 4.
Nomograms for determination of initial concentrations of ethanol in fluoroplastic containers

Results of modeling the process of decline of concentrations in containers

Container No	Substance	a	b
1	Methanol	0.7991	—0.1140
2		0.7487	—0.1319
3		0.7013	—0.1159
4		0.7299	—0.1606
1	Acetone	1.1264	—0.2261
2		1.1054	—0.2314
3		1.0113	—0.2279
4		1.0561	—0.2731
1	Ethanol	1.1256	—0.0845
2		1.0571	—0.0521
3		1.0340	—0.0446
4		0.9832	—0.0536
1	Ethyl acetate	1.2529	—0.1645
2		1.3877	—0.3504
3		1.3124	—0.3328
4		1.3663	—0.2069

We constructed the log-linear regression model using the least squares method [2, 3]. We obtained functions with the following appearance:

$$\log (k) = b \cdot \log (t) + a \quad (1)$$

where a and b are coefficients in the equation of log-linear regression, a characterizing the concentration of a substance at the start of collection of a sample and b showing the rate of decline of concentration during storage; log (k) and log (t) are logarithms of concentration and time.

The table lists the values of coefficients a and b for the tested organic substances. We calculated Fisher's criterion and level of significance of P (in all of the containers, $P<0.5$ for ethanol, $P<0.01$ for methanol, acetone and ethyl acetate).

On the basis of the obtained functions, we plotted nomograms (Figure 4) for each container, which enabled us to determine the initial concentration of a substance by measuring its containers [volumes?] on any day.

In order to obtain an overall expression for each substance, we standardized the base data.

An expression of the following general form was obtained:

$$\log \frac{k}{k_0} = b \cdot \log (t) \qquad (2)$$

where b is the coefficient of the equation of log-linear regression, log (t) is the logarithm of time, k is the measured concentration at moment t and k_0 is the initial concentration of a substance.

Coefficients b in equation (2) had the following values for the tested substances: 0.229 for acetone, 0.120 for methanol, 0.0654 for ethanol and 0.262 for ethyl acetate.

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AGE-RELATED CHANGES IN BODY AND VISCERAL WEIGHT OF WISTAR RATS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 6 May 80) pp 79-81

[Article by G. I. Plakhuta-Plakutina, Ye. I. Alekseyev, G. N. Durnova, Ye. I. Il'ina-Kakuyeva, A. S. Kaplanskiy, A. S. Pankova, Ye. A. Savina, V. N. Shvets and V. I. Yakovleva]

[Text] When conducting experiments on animals, researchers use such integral parameters as body weight, absolute and relative weight of internal organs, endocrine glands, muscles and bones. Relative organ mass is determined when it is necessary to compare the results of experiments conducted on animals differing in body mass. Yet there are some limitations to the use of this parameter, particularly when such constantly growing animals as rats and mice are used in experiments, in whom there could be a substantial change at different stages of postnatal life in correlation between body weight and that of different internal organs due to irregular increase thereof. Apparently, one must know the relative weight of viscera of normal animals of the same age in order to assess changes in this parameter. At the same time, the information in the literature concerning age-related norms for viscera and tissues of laboratory animals was extremely limited [1-4]. This prompted us to investigate the patterns of growth of the body, absolute and relative weight of internal organs, endocrine glands, different muscles and linear parameters of the skeleton.

Methods

We used 160 male Wistar rats obtained from the Stolbovaya [laboratory animal] vivarium at the age of 30 days. The animals were kept on the usual diet in our vivarium. We sacrificed 12-15 animals at a time by means of ether anesthesia every 10 days in the course of the 110-day experiment, and dissected them. We paid special attention at dissection to the presence of spontaneous pathology; we measured body weight, length of the body, tail and some bones of the limbs, as well as absolute and relative weight of viscera, endocrine glands and some muscles. Relative growth rate (increment) of the body and internal organs was determined with the formula [5]:

$$\frac{V_2 - V_1}{V_1} \cdot 100\%$$

Bone length was measured with calipers to the nearest 0.01 mm. The material was submitted to statistical processing with the use of Student's criterion.

Results and Discussion

The animals' general condition was satisfactory throughout the experiment. Nevertheless, the postmortem revealed otitis in a significant number of rats. Otitis was demonstrable in virtually all animals at 30 or more days of age. Microfocal pneumonia was demonstrated in rats at later stages of postnatal development (after 80 days). On the whole, the incidence of pneumonia constituted 7.5% and otitis 69% of the 160 animals examined. We failed to demonstrate spontaneous diseases at the postmortem.

As can be seen from the data listed in Table 1, an increase in body mass, body and tail length was noted throughout the period of studying the animals. The rats grew the most intensively up to the age of 2-2.5 months, after which there was slower increase in body weight, body and tail length.

Table 1. Age-related changes in weight of body and internal organs of rats (M±m)

Age, days	Body wt., g	Length, cm		Mass, mg (mg/g)					
		body	tail	heart	spleen	kidneys	liver	lungs	brain
30	79±3	15.6	12.0	379±14 (4.8±0.18)	347±25 (4.4±0.32)	835±21 (11.0±0.9)	3 556±170 (45±0.9)	713±15.4 (9.0±0.2)	1542±11 (19.9±1.3)
40	164±4	19.3	14.7	682±18 (4.2±0.06)	744±50 (4.5±0.26)	1462±37 (8.9±0.1)	8 200±280 (50±0.97)	1229±50 (7.5±0.2)	1670±25 (10.2±0.2)
50	225±6	21.1	16.3	871±50 (3.9±0.07)	756±52 (3.5±0.19)	1918±70 (8.5±0.2)	10 700±469 (48±0.93)	1620±60 (7.2±0.3)	1771±29 (7.9±0.2)
60	274±9	23.5	17.0	1055±35 (3.9±0.11)	781±66 (2.8±0.20)	2190±104 (8.0±0.2)	11 723±516 (43±0.55)	1740±46 (6.4±0.2)	1812±27 (6.7±0.2)
70	292±12	23.8	17.6	1021±36 (3.5±0.06)	740±37 (2.6±0.15)	2353±88 (8.0±0.2)	11 683±744 (40±0.98)	1614±63 (5.5±0.2)	1829±35 (6.3±0.1)
80	344±11	24.8	18.5	1133±32 (3.3±0.06)	758±34 (2.2±0.09)	2750±60 (8.0±0.3)	15 542±453 (45±0.99)	1917±65 (5.6±0.2)	1965±23 (5.7±0.1)
90	371±12	25.2	18.8	1118±34 (3.2±0.05)	795±29 (2.1±0.08)	2922±115 (7.6±0.2)	17 320±897 (47±0.98)	2109±83 (5.7±0.3)	1972±19 (5.5±0.1)
100	379±12	24.5	19.2	1235±28 (3.3±0.06)	814±30 (2.1±0.05)	2823±150 (7.4±0.2)	17 545±933 (46±1.8)	2000±60 (5.3±0.2)	1972±30 (5.5±0.1)
110	406±11	24.7	20.0	1227±46 (3.0±0.06)	878±34 (2.2±0.06)	2814±93 (6.9±0.1)	18 162±777 (45±1.3)	2012±65 (5.0±0.1)	1974±13 (4.9±0.1)
120	399±17	24.3	20.2	1303±57 (3.3±0.09)	806±38 (2 ±0.09)	2967±153 (7.5±0.3)	16 986±894 (43±1.1)	2346±122 (5.9±0.5)	2031±31 (5.2±0.2)
130	463±16	25.2	20.3	1321±38 (2.9±0.05)	9 3±36 (2.0±0.08)	3461±139 (7.5±0.2)	20 947±916 (45±1.2)	2620±112 (5.6±0.2)	2094±18 (4.5±0.2)
140	493±15	27.9	20.4	1376±44 (3.0±0.01)	893±33 (1.8±0.06)	3209±86 (6.5±0.1)	20 161±809 (41±0.9)	2139±77 (4.9±0.2)	2062±23 (4.2±0.1)

Note: Here and in Tables 2 and 3, relative mass (mg/g) is given in parentheses.

There was rapid increase in absolute weight of the heart, liver, kidneys, lungs, pituitary, thyroid, adrenals and testes between the 30th and 60th days of postnatal development (Tables 1 and 2). Thus, increment constituted 230% for liver mass at this time, 178% for the heart, 162% for the kidneys, 273% for the testes, 167% for the thyroid, 135% for the hypophysis and 112% for the adrenals. In this period, the weight of the brain increased by only 17%, from which we can assume that the most active rise of this parameter occurred at prior stages of ontogenesis. There was drastic increase in absolute weight of the thymus and spleen in the 30th-40th days of life. After this, the spleen continued to increase in weight, but more slowly, whereas the weight of the thymus remained constant up to the age of 70 days, after which it gradually decreased. Thereafter, as the animals grew older, the absolute weight of internal organs continued to increase, whereas there was virtually no change in weight of endocrine glands after the age of 3 months (mean increment did not exceed 5%; see Table 2).

Table 2. Age-related changes in mass of rat endocrine glands (M±m)

Age, days	Mass, mg (mg/g)				
	thymus	adrenals	thyroid	pituitary	testes
30	195±7 (2,5±0,1)	18,2±0,7 (0,23±0,014)	8,6±0,6 (0,11±0,006)	3,96±0,19 (0,050±0,001)	384±16 (4,9±0,17)
40	515±27 (3,1±0,1	27,0±0,83 (0,16±0,002)	15,1±0,5 (0,09±0,003)	6,4±0,27 (0,039±0,0013)	883±19 (5,4±0,14)
50	522±36 (2,4±0,15)	32,5±1,4 (0,14±0,006)	20,0±1,008 (0,09±0,005)	7,9±0,36 (0,036±0,002)	1195±20 (5,3±0,09)
60	539±34 (1,9±0,1)	38,3±1,6 (0,14±0,005)	23,0±0,7 (0,08±0,004)	9,3±0,4 (0.034±0,001)	1433±31 (5,2±0,15)
70	488±18 (1,7±0,1)	52,4±1,9 (0,18±0,005)	31,7±1,85 (0,11±0,006)	10,8±0,27 (0,037±0,0013)	1589±32 (5,4±0,2)
80	374±40 (1,1±0,1)	50,2±2,0 (0,15±0,005)	33,3±1,02 (0,10±0,008)	12,2±0,44 (0.035±0,0017)	1654±46 (4,8±0,16)
90	383±33,0 (1,0±0,08)	47,8±3,0 (0,13±0,004)	39,8±1,3 (0,11±0,001)	11,3±0,38 (0,030±0,001)	1737±39 (4,6±0,14)
100	342±17 (0.9±0,04)	44,5±2,1 (0,12±0,005)	38,4±0,5 (0,10±0,002)	10,8±0,64 (0,028±0,008)	1727±35 (4,6±0,17)
110	350±24 (0,9±0,04)	47,4±2,3 (0,12±0,006)	39,4±2,1 (0,10±0,005)	12,2±0,65 (0,030±0,001)	1660±28 (4,1±0,13)
120	298±20 (0,8±0,05)	50,1±3,1 (0,13±0,005)	36,0±2,5 (0,09±0,006)	10,1±0,57 (0,025±0,001)	1671±41 (4,2±0,25)
130	372±24 (0,8±0,06)	59,8±2,3 (0,13±0,005)	39,7±1,38 (0,09±0,005)	11,9±0,58 (0,026±0,001)	1775±43 (3,8±0,18)
140	299±20 (0,6±0,05)	51,0±1,95 (0,103±0,004)	41,3±1,62 (0,08±0,004)	11,7±0,28 (0,024±0,008)	1764±45 (3,6±0,14)

Table 3. Age-related changes in muscle mass (M±m)

Age, days	Muscle mass mg (mg/kg)					
	soleus	gastroc-nemius	anterior tibia	extensor digitorum longus	femoral quadriceps	brachial biceps
30	35,8±1,07 (0,45±0,01)	354,5±9,4 (4,51±0,06)	136,2±5,23 (1,73±0,02)	35,4±1,38 (0,44±0,01)	461±14,6 (5,87±0,17)	89±3,84 (1,12±0,13)
40	62,7±2,4 (0,37±0,006)	832,5±19,4 (5,06±0,06)	293,5±10,2 (1,77±0,03)	74,3±2,95 (0.44±0,01)	1041±32,3 (6,26±0,14)	208,5±10,0 (1,26±0,04)
50	84,9±2,58 (0,37±0,006)	1158±32,36 (5,13±0,1)	382,7±10,0 (1,69±0,04)	94,1±3,32 (0,41±0,009	1313,6±42,53 (5,83±0,1)	210,8±6,52 (0,92±0,02)
60	104,9±2,84 (0,38±0,008)	1484,6±42,35 (5,42±0,1)	502,6±11,93 (1,84±0,04)	126,0±3,61 (0,45±0,01)	1876,0±57,7 (6,84±0,08)	339,6±13,0 (1,23±0,033)
70	112,8±6,38 (0,37±0,01)	1566±73,9 (5,35±0,1)	516,6±24,0 (1,76±0,03)	121,6±4,9 (0,41±0,006	1985,0±93,4 (6,79±0,1)	352,6±14,6 (1,20±0,056)
80	137,0±5,0 (0,39±0,007)	1937,0±70,2 (5,74±0,12)	625,0±20,3 (1,81±0,04)	151,8±5,27 (0,43±0,01)	2424,0±79,5 (7,05±14)	324,2±14,6 (0,93±0,03)
90	162,8±4,85 (0,43±0,01)	2152,6±46,9 (5,08±0,1)	822,6±26,1 (2,21±0,04)	189,8±4,92 (0,50±0,01)	2752,0±69,3 (7,43±0,16)	481,5±11,9 (1,30±0,02)
100	121,4±2,79 (0,31±0,006)	2180,9±95,7 (5,74±0,11)	743,6±22,9 (1,95±0,01)	187,0±7,08 (0,48±0,01)	2650,0±108,7 (6,99±0,17)	430,9±11,57 (1,13±0,01)
110	132,0±6,9 (0,31±0,01)	2166,6±72,1 (5,34±0,1)	735,0±33,3 (1,79±0,05)	178,0±5,45 (0,43±0,01)	2929,1±106,3 (7,21±0,15)	491,08±20,7 (1,20±0,03)
120	156,3±6,0 (0,39±0,01)	2212,8±101,1 (5,54±0,09)	710,7±36,5 (1,77±0,04)	164,7±7,0 (0,40±0,01)	2962,1±108,9 (7,45±0,18)	376,9±16,59 (0,94±0,02)
130	155,2±6,54 (0,33±0,01)	2458,0±132,4 (5,30±0,23)	816,6±30,8 (1,76±0,04)	188,8±6,62 (0,40±0,008)	3064,6±119,3 (6,64±0,18)	436,4±20,9 (0,94±0,03)
140	148,6±5,53 (0,29±0,007)	2361,4±69,9 (4,81±0,11)	772,1±22,7 (1,57±0,05)	192,2±4,71 (0,38±0,009)	3212,5±91,8 (6,54±0,25)	443,2±14,6 (0,90±0,02)

There was rapid decline of relative mass of most internal organs and endocrine glands between the 30th and 60th days of life, which was related to the intensive increase in body weight, which exceeded significantly the increase in visceral weight. From the 80th day of postnatal development, there was some stabilization

of relative weight of internal organs and endocrine glands: the decrease in relative mass of all organs without exception occurred very slowly (see Tables 1 and 2).

Table 4.
Rat bone length increment (mm/day) as a function of age

Bone	Age, days			
	30—60	60—90	90—120	120—140
Femur	0,32	0,08	0,08	0,02
Tibia	0,33	0,12	0,04	0,05
Humerus	0,21	0,10	0,05	0,03
Ulna	0,22	0,10	0,06	0,06
Radius	0,20	0,08	0,06	0,01

While the absolute mass of internal organs increased the most rapidly between the 30th and 60th days of life, absolute mass of muscles of the hind legs continued to increase rapidly up to the 90th day. After this time, we observed relative stabilization of mass of the soleus and anterior tibial muscles, as well as the extensor digitorum longus and brachial biceps, whereas the mass of the gastrocnemius and femoral quadriceps continued to increase. We failed to demonstrate consistent changes in relative mass of muscles as a function of age of the animals (Table 3).

The results of measuring the length of the anterior and posterior extremity revealed that growth thereof did not stop throughout the experiment, while the growth rate depended on the age of the rats. According to the data listed in Table 4, there was the fastest increase in length of bones of the front and hind legs up to the age of 60 days, after which it drastically diminished. A comparison of parameters of bone length to body weight and rat age revealed that this parameter can be related to both the age of the animals and their weight.

The results of our study indicate that rats grow the most intensively up to the 80th-90th day of postnatal ontogenesis. Thereafter, growth slows down and, starting in the 3d month of life when there is some stabilization of relative weight of internal organs, the animals can be considered to be adults. On this basis, it is deemed desirable to use animals from the age of 3 months in experiments conducted to investigate the effects of various extreme factors on the adult organism. It is expressly stabilization of relative weight of internal organs and endocrine glands, rather than reaching puberty, which occurs in rats at about 2 months of age [6], that is one of the criteria of completion of development of the animals. The existence of substantial variations of body weight, absolute and relative weight of internal organs of rats of the same age warrants the belief that body weight cannot serve as the sole criterion, and when selecting animals it is imperative to make sure that rats are not only of the same weight, but the same age. When using rats in experiments that have not reached adulthood, each experimental group must correspond to its own control group, since a difference in age, even of a few days, could cause substantial error of such parameters as absolute and relative body and visceral mass. It must also be borne in mind that, during the period of intensive growth of rats, the effects of extreme factors and, in particular, their influence on visceral mass could be cancelled out by the rapid growth of the organ under study.

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METHOD OF TESTING WHITE RAT ELEVATOR RESPONSE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 2 Feb 80) pp 82-84

[Article by G. S. Ayzikov, A. S. Markin, A. V. Mokrousova and I. Yu. Sarkisov]

[Text] Studies were made of the latency period of the elevator reaction (LPER) in order to analyze the state of vestibulomotor reactions of animals following long-term space flights aboard Cosmos-936 [1] and Cosmos-1129 biosatellites. This reaction is a variant of otolithic-spinal reflexes, which occur in response to vertical motion. In the case of free fall, the elevator response is manifested in animals by drastic extension of the limbs, elevation of the head and drastic bending of the back. Such a reaction is usually evaluated clinically, and it is used to determine the integrity of dynamic otolith function [2-4]. The LPER can be determined by the methods in [5-7]; however, this parameter is recorded with some element of error because of the distinctive design features of devices that rock [5] or drop [6] an animal. The method described in [7] is more reliable. However, it has limited applications, since, in the first place, it involves implantation of electrodes in muscles, which is not feasible in a number of experimental situations, and in the second place the LPER is recorded on animals that were deprived of contact with a surface [support] initially, which alters appreciably the functional state of the vestibular system [8].

We refined the methods in [5-7] and developed a device to study the LPER of white rats, in accordance with the program of inflight experiments aboard Cosmos-936 and Cosmos-1129, as well as in order to improve the accuracy and reproducibility of test results.

The device (Figure 1A) consists of an animal container *1*, vertical guide rod *2*, movable platform *3*, on which container *1* is placed, shock-absorber unit *4* and recorder *5*. Container *1* is variable in size and made of plexiglas (Figure 1B). The size is regulated by moving lid *6*, which is secured at a specified distance from the floor, and sliding wall *7* with screw connection *8*. One side of lid *6* is attached to the container wall with an axial joint and can be rotated, the other side rests on a magnetic holder by means of iron plate *9* and connects the "lobes" [prongs?] of electric contact *10*. The axial joint [connection] of lid can be secured at any distance between container *1* and the floor. The magnetic holder *9*, together with electric contact *10* can be moved vertically, analogously to the axial joint of lid *6*, and when making an individual choice of height of container *1* lid *6* can always retain a horizontal position. The force with which the magnetic holder *9* holds the lid (~175 g) is so selected that the animal is able to lift it only by extending its limb. The possibility of the lid opening

due to chance jolts, vibration and contact is entirely ruled out, and a standard resistance is created, to overcome which a muscular effort must be made. This permits recording the LPER according to the motor effect, which occurs under unchanging test conditions. If necessary, the magnetic holding force is adjusted by altering the mass of the contacting pair of magnets--the iron plate or by installing another magnet with the required characteristics. Guide rod *2*, which is 180 cm in height, has casters so that it can be rolled over the laboratory floor. Shock-absorber unit *4* consists of a multilayered set of porolon and rubber liners, which are alternated in the bottom part of guide rod *2*. Because of this, platform stops smoothly and without impact after it drops. There is an electric magnet in the top part of guide rod *2* to suspend and drop platform *3*. There are slots in the platform so that several animal containers *1* can be installed and secured on it at the same time. Platform *3* moves freely along guide rod *2* by means of a lining with fluoroplastic bearings. An electronic pulse counter is used as the device to record the LPER. When several animals are tested at the same time, the LPER of each rat is measured either with individual counters, one of which is illustrated in Figure 1, or with an analogous multichannel instrument with independent disconnection of time measuring channels.

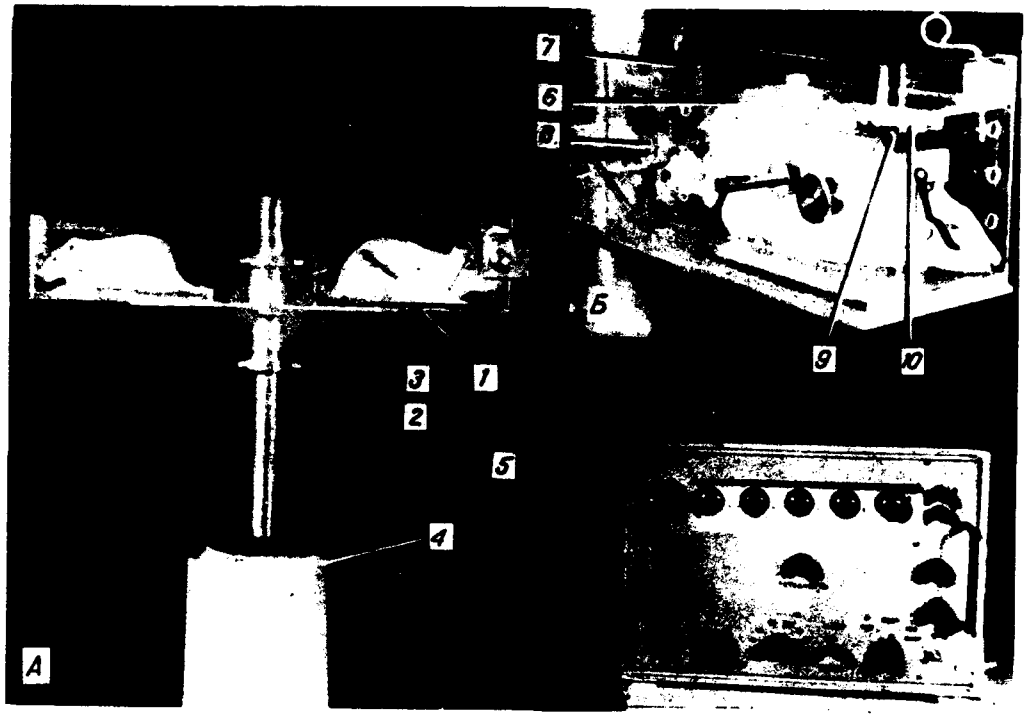

Figure 1. General view of device for studying the elevator reaction of laboratory animals. Explanation given in the text.

The device operates in the following manner. A rat is placed in container *1*, the size of which can be easily adjusted to the size of the animal to preclude any turning around and provide standard testing conditions. Container *1* is lifted on platform *3* and placed in the top part of guide rod *2* by means of the electromagnet. At the proper time, the experimenter turns the electromagnet off and platform *3* falls under the influence of gravity, then it is stopped by the shock-absorber unit *4*. At the start of the fall, the pulse counter is turned on by a triggering device, which disconnects the power of the electromagnet, and the counter starts to mark the time. The animal, reacting to the fall by extending its limbs, raises the container lid, as a result of which the electric contact is broken and measurement of LPER stops. The LPER is recorded on the dial of the instrument (in milliseconds). In our experiments, the normal value of this parameter constituted 28±6 ms for Wistar-SPF white rats weighing 200-250 g. After obtaining reference LPER values, we standardized the experimental conditions as much as possible. Animals were used in the experiment 2-3 h after feed intake; they were gradually adapted to the test conditions (to the laboratory situation and staying in the container). The container lid was always placed horizontally and right on the back of the prone animal. The platform was dropped with the animal in calm, waking state. The results of 10 successive drops at randomized intervals (at least 4-5 min) were averaged, while the data for the entire series (60 animals) were submitted to statistical processing by the weighted mean method.

In our method, the LPER is the overall parameter caused by passage of vestibular impulsation over numerous and functionally different parts of the nervous system. It included the time of appearance of a vestibular impulse, time of travel over nerve fibers of at least five synaptic lags and time of development of sufficient muscular exertion to overcome the resistance of the magnetic holder. In general, the reflex pathway was as follows: otolith receptors--vestibular nerve--vestibular nuclei--vestibulospinal tract--spinal cord--motor nerves--muscular contraction involved in the last phase of the elevator reaction. The latter has a significant influence on magnitude of the LPER, since participation in a space flight worsens substantially the characteristics of a muscular contraction [9], whereas spinal reflexes and conduction time over nerves remain virtually unchanged [10]. It was extremely important to determine the role of the vestibular and motor components of the reflex in the aftereffect period following the space flight. It is also possible to use this device for such determination by means of additional evaluation of LPER according to the electromyographic responses of muscles, for example, the gastrocnemius and oculomotor muscles. For this purpose an interchangeable container is provided with the device, which is of the open type and has equipment to immobilize the rat's head and trunk. In our experiments, we used bipolar needle electrodes inserted in the region of the outer edge of the orbit [canthus?] and belly of one of the gastrocnemius muscles. After preamplification, the electromyographic responses were recorded from the screen of a cathode oscillograph. The beam was turned on at the moment the platform was dropped, at the

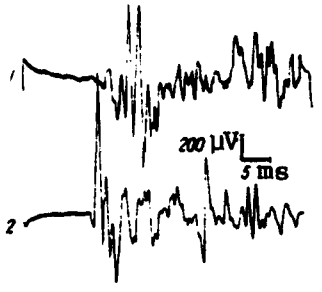

Figure 2.
Electromyographic responses in the elevator reaction. Calibration signal: 200 μV--5 ms.
1) gastrocnemius reaction
2) oculomotor muscle reaction

signal that the electromagnet was off. Normally, in white rats on the usual vivarium upkeep, the LPER constituted 14.3±0.4 ms for oculomotor muscles and 17.8± 0.4 ms for the gastrocnemius, as determined by the first spike on the electromyogram. The differences were reliable for a significance level of $P<0.001$. The experimental conditions and composition of experimental material were analogous to those described above. Figure 2 illustrates samples of electromyographic responses in the elevator reaction, and it shows that the burst of electromyographic activity after dropping the container with an animal occurs against the background of bioelectrical silence, and the LPER is not the same for the oculomotor and gastrocnemius muscles.

The device described is low in weight (5-7 kg), it can be disassembled and is designed to operate under field conditions.

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UDC: 615.472.5:612.13-087.8

SUBCUTANEOUSLY IMPLANTED CONNECTOR TO RECORD ARTERIAL PRESSURE AND MAKE ELECTRICAL CONTACT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug (manuscript received 28 Nov 80) pp 84-85

[Article by Yu. Ya. Ganich, V. S. Baranov, V. V. Suchkov and O. S. Medvedev]

[Text] Studies of central and peirpheral mechanisms of hemodynamic regulation in nonanesthetized normotensive and hypertensive animals present the problem of being able to reliably record blood pressure in chronic experiments. In previously published works, it was suggested that the distal end of a catheter be connected to a valve attached to the skull [1, 2] and to close it with a metal or plastic plug [3-5]. The common flaw of the described designs is that the distal end of the catheter is outside the animal's body, which involves the possibility of damage to the catheter or its being pulled out by the animal; moreover, there is the constant danger of an inflammatory process in the area where the catheter is passed through the skin.

The catheter design that we propose, with a nipple connector on the end, makes it possible to avoid these complications, since the catheter is completely implanted under the skin. The connector could, with minor alteration of design, be used to provide temporary electrical contact, which is sometimes necessary when recording biopotentials or for electric stimulation.

The construction of the union nipple for a vascular catheter is illustrated in Figure 1. Disposable polyethylene venous catheters with a tapered connector at the end for a syringe serve as the base equipment. It is best to use catheters that are designed to be connected with Luer type syringes. A plug made of silicone rubber is placed tightly into the tip, after which the edges are slightly rolled with the tip of a hot soldering iron.

Before implantation, the catheter is sterilized in alcohol or diocid solution, then filled with heparin solution, the viscosity of which is increased by adding gelatin or polyvinylpyrrolidone. Insertion of the catheter is performed under general anesthesia. After securing the catheter with ligatures, the incision is sutured in layers so that the union nipple is just under the skin, to one side of the suture.

Animals are used for experiments 2-3 days after implanting the catheter. The skin is punctured with an injection needle in the region of the union nipple for connection thereof to the catheter, and then the nipple connector. The injection

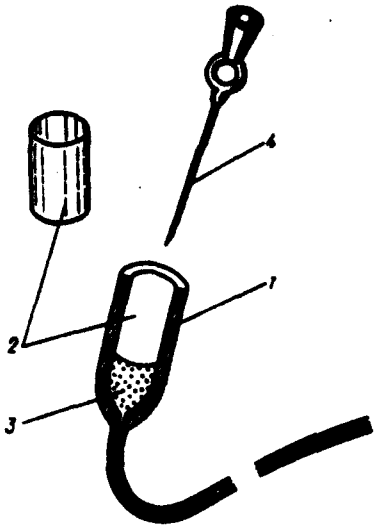

Figure 1.
Construction of union nipple
1) polyethylene housing of connector
2) plug of silicone rubber
3) inside of connector with heparin
4) injection needle

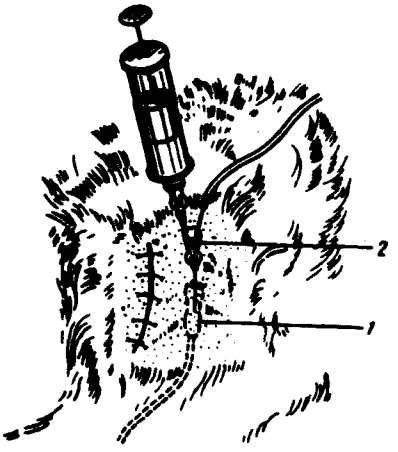

Figure 2.
Drawing of connection to implanted catheter by means of needle with nipple
1) subcutaneous connector with nipple
2) connecting needle with nipple

needle itself also has a nipple, so that only one puncture of the skin has to be made during an experiment, and repeated attachment of a syringe for injections, taking blood samples, giving agents and connecting the electric pressure gauge are performed through the needle's nipple connector. Such a dual union nipple is illustrated in Figure 2.

Such catheters were used for 3 years in experiments on rabbits. As shown by tests and microbiological analysis, no growth of microflora was observed provided sterile conditions were maintained inside the nipple connector, and there was not a single case of damage to the catheter caused by the animal or development of inflammation in any of the experiments.

By virtue of mobility and elasticity of the skin, the surface punctured by the injection needle for attachment to the union nipple is rather large (10-22 mm in diameter), so that there is no trauma to the circumscribed skin region.

A comparable principle of implanted connector was used to make temporary electric contact. For this purpose, the polyethylene tube of the catheter was clipped at a distance of 5-10 mm from the tip. The end of an electric conductor was inserted in the tube and the point of contact was covered with polyethylene or special adhesive. The protected [insulated?] part of the conductor in the tip was covered with mercury (provided the material of the conductor did not form an amalgam with mercury) or connected to a stopper made of conducting silicone rubber, closed at the top with ordinary silicone rubber. Thus, the connector ready for implantation was entirely insulated from surrounding tissues. The needle used to puncture the skin was coated with insulating varnish over its entire length, with the exception

of the point, which was pushed through the plug to make contact with the conducting material of the connector.

The use of the above-described hydraulic and electric implantable connectors is particularly indicated for chronic experiments (lasting 1 month or longer), since this preserves the catheter and electrodes, and prevents contact spread of infection along the catheter.

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UDC: 612.822.3.014.421:57.082

METHOD FOR ATTACHING CEREBRAL THERMOCOUPLE WIRES TO THE DOG'S SKULL

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 12 Sep 80) pp 85-86

[Article by O. Ye. Ozerova]

[Text] Researchers involved with the study of various functions of the animal brain are well aware of the difficulty involved in attaching sensors to the skull of an animal, so that they could be used for a long period of time. This task is even more difficult when recording brain temperature, since a mandatory prerequisite for this is to preserve the skull's natural heat insulation.

In earlier designs known to us [1, 2], the securing device was situated directly on skull bones without periosteum. This enhanced the effect of the ambient environment on brain temperature.

Our objective here was to develop a method for attaching brain thermocouple wires to the dog's skull, which would make it possible to retain natural heat insulation of the brain.

We made use of the idea of Hayward and Baker [3], which consisted of using a "shoe" [chock, block?] to secure a thermocouple situated over the animal's skull (Figure 1). The two parts used to secure the brain thermocouple wires are illustrated in Figure 2. The thermocouple wires were situated in a box attached to the skull by means of chrome-plated steel wood screws, while a round platform on legs was used as a device or guide to insert [screw in] the wood screws into the dog's skull bone. The location of holes in the round platform corresponded exactly the their location at the bottom of the box. The wood screws were prepared in the following manner: the top of the screw was cut off so that the remaining part without thread would be 9 mm longer than the height of the leg of the guide. Then it was threaded for a nut at a depth of 10 mm from the top. A threaded bushing with a screw head was made to screw the wood screws into the skull bone (hereafter, we shall refer to this part as the "head"); the length of threading on the bushing was 5 mm.

All of the manipulations related to the use of the proposed method were performed with animals under general anesthesia (5-7 mℓ droperidol and 70 mg/kg nembutal). First, we made an incision in the scalp in the middle of the head and spread the edges to either side. Then we placed the round platform on the skull; in places where the legs of the platform came in contact with muscles, we severed the latter and exposed the skull. We made trephination holes through the legs

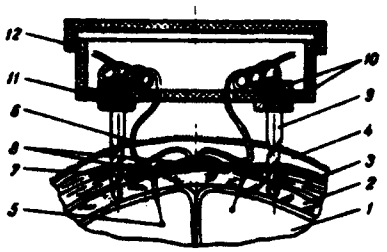

Figure 1.
Diagram of location of wires going from thermojunctions implanted in the brain and attachment thereof by means of the box,

1) brain
2) bone
3) muscle
4) skin
5) thermojunction
6) thermojunction wires
7) wooden wedge
8) noracryl
9) wood screw
10) nut
11) lid

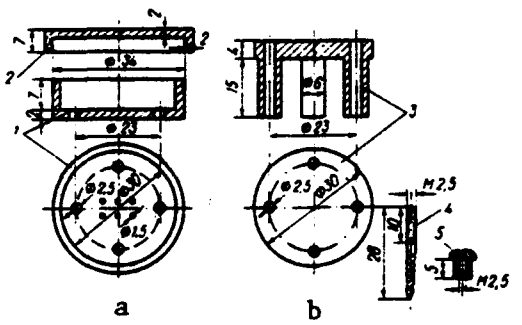

Figure 2.
Box for attachment of wires from thermojunctions to dog's skull (a) and device (guide) for screwing in the wood screws (b)

1) box
2) lid
3) guide
4) wood screw
5) head

of the guide, which was placed on bone wanting in periosteum. Through these holes we inserted the wood screws to the stop at the base of the guide, using the head. The head was then removed and the legged platform was removed by an upward movement.

Thermojunctions coated with plexiglas were inserted through the trephination holes to implant thermocouples in the dog's brain. The openings were then closed with wooden wedges and covered with noracryl [?].

According to the data of A. I. Arutyunov and N. V. Semenov [4], the wires from the thermojunction must be placed "in isotherm, i.e., parallel to the skin surface," over a specific distance. In view of these recommendations, we passed the thermojunction wires from the trephination holes to the sagittal suture on both sides of the skull, in the region of which they were attached to the bone with noracryl, and they were then passed 1.5 cm to the right and left, where they were stitched to muscles with silk (see Figure 1). Incisions were made in the skin in these places, as well as projections of the wood screws, through which the thermocouple wires and wood screws were brought out. After this, we sutured the muscles, fascia and scalp; we did not shave the fur off the head. Then, we screwed a stop nut on each wood screw, placed the box on the nuts and then screwed on lock nuts on all of the screws inside the box. After this, the thermocouple wires were pulled into the box through the holes in its bottom, and the lid was screwed on top of the box. The height of placement of the box over the dog's skull could be changed by virtue of the fact that the thread extended over 10 mm on the guide [support] wood screw, by the position of the nuts. This had to be done when the length and thickness of the coats of different animals differed. The method we used permits retention of natural head insulation of the animal's skull, as we have noted above. It was used on 15 mongrel dogs in a study of normal temperature conditions of the brain. We worked with each animal for 1 to 1.5 months. During this time, the thermocouple wires and attaching device remained intact, in spite of the diverse and intensive movements of the dogs. The method we propose for attaching thermocouple wires is also suitable with the use of

other sensors. This permits investigation of various functions of the animal brain for a long period of time and with intact natural heat insulation of the skull.

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BRIEF REPORTS

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SIGNIFICANCE OF HEMATOLOGICAL CHANGES IN RESISTANCE TO DECOMPRESSION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 5 Jun 79) pp 87-88

[Article by V. V. Vlasov]

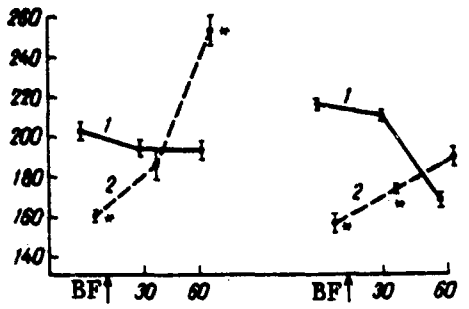
[Text] We can expect that the screening of people resistant to decompression will not only increase the efficacy of existing measures for the prevention of caisson disease, but prevent the long-term adverse sequelae of oversaturation of the body with a neutral gas (diseases of the nervous and cardiovascular systems, aseptic osteonecrosis [1, 2]). According to previously published data [3, 4], resistance to decompression is related to the cellular composition and state of the coagulating system of blood. We previously demonstrated [5] that hypocoagulation, which enhances resistance to gas embolisms, develops in animal blood after intravenous injection of air. We have tried to determine here the significance of the initial state and of some changes in the blood system in the presence of artificial gas embolism in animal resistance to decompression.

Methods

Experiments were conducted on male rabbits weighing 1500-3800 g. At the first stage of the experiments, to 66 rabbits 1 cc air was injected in the lateral auricular vein within 15 s in order to test the blood reaction to a graded volume of intravascular gas phase. After 7-8 days, at the second stage of the experiments, the rabbits were exposed to air pressure of 6 kg/cm^2 for 16 min, after which decompression to normal pressure was performed in 2 min. We found that 16 out of 36 animals were not resistant to decompression. They developed the disease in the form of transient dyspnea. At the third stage of the experiments, a massive gas embolism was produced in 13 rabbits. We injected in the auricular vein of these animals 1 cm^3 air for 15 s at 30-s intervals until the animals developed seizures. We assessed resistance to the massive gas embolism by the dosage of injected air referred to body weight. Blood for tests was taken from the lateral vein of the ear before the experiment, 30 and 60 min after injection of air in the vein of the contralateral ear or decompression. We assayed the leukocyte formula on the day after taking blood. We tested blood for cellular composition, levels of free fatty acids, total cholesterol, total lipids and β-lipoproteins [6]. Coagulation of blood was evaluated by electrocoagulography.

Results and Discussion

Decompression and graded artificial gas embolism elicited similar changes in blood properties. After these factors, there was a decrease in blood β-lipoprotein



Gas embolism Decompression

Changes in blood serum total lipids in rabbits with gas embolism and after decompression. X-axis, time after use of factor (min); y-axis, blood serum total lipids (mg/100 mℓ).
BF) before
1,2) decompression resistant and non-resistant animals, respectively
*) reliable (P<0.05) differences between resistant and non-resistant animals

(P<0.05) and cholesterol content. At first, the concentration of nonesterified fatty acids of blood serum decreased, then increased. However, other parameters of blood changed in the opposite directions in decompression resistant and nonresistant animals.

In decompression-resistant rabbits, blood lipid levels decreased with the use of both factors, and in the presence of insignificant hypolipemia there was already intensification of hypocoagulation; in nonresistant animals, on the contrary, lipid levels rose; this was associated with faster blood clotting and increased clot thickness (see Figure). Hyperlipemia and hypercoagulation worsen the microcirculatory disturbances related to presence of intravascular gas bubbles and aggregation of blood cells, which leads to slower desaturation of tissues from a neutral gas and intensification of gas production.

Moreover, basophilopenia (P<0.05) developed in decompression-resistant animals, and there was a decline of hematocrit (P<0.05, according to maximum amplitude of the electrocoagulogram). The hematocrit decline is apparently a protective reaction, and it is consistently observed in man after decompression when not associated with development of disease [7].

In animals that are not resistant to decompression, there was development of leukopenia (P<0.05), chiefly referable to neutrophils (P<0.05) and monocytes (P<0.05); there was also thrombocytosis (P<0.05) with subsequent thrombocytopenia (P<0.05); we observed a tendency toward lymphopenia and increase in hematocrit. These changes were indicative of a very marked reaction of blood to the foreign (gas) surface. The transient increase in peripheral blood thrombocyte count could be related to discharge thereof from their reservoir (lungs) under the influence of gas embolisms [8].

These studies revealed that the base state of animals without resistance to decompression differed from those with resistance in that there was relative leukocytosis (P<0.05), fewer basophils, many monocytes and lymphocytes, relative hypocoagulation (P<0.05), activation of fibrinolysis (P<0.05), hypercholesterolemia and hypolipemia (P<0.05). It can be expected that preliminary assay of these parameters would permit prediction of resistance to decompression. At the same time, in our experiments, animals without resistance to decompression tolerated a massive gas embolism somewhat better (3.72±0.73 cc/kg, versus 2.32±0.38 cc/kg in decompression-resistant ones; P>0.05).

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EFFECT OF HYPOXIA ON AFFINITY OF HEMOGLOBIN FOR OXYGEN IN ANIMALS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 31 [sic] Sep 80) pp 88-89

[Article by V. V. Gladilov]

[Text] Among factors that regulate affinity of hemoglobin for oxygen (AHO), a special place is held by 2,3-diphosphoglycerinic acid (DPG). However, the level of this phosphate in the blood of animals of different species and age is not the same, as a result of which we can expect different hemoglobin reactions to hypoxia of the organism.

Methods

In our tests, we used blood from mongrel cats and rabbits of both sexes and different age, as well as adult golden hamsters. Hypoxic conditions corresponding to altitudes of 5000 and 7000 m were created in a 60-ℓ pressure chamber for 1 h. The curves of dissociation of oxyhemoglobin were obtained by spectrophotometry [1]; glucose content was assayed by the conventional clinical orthotoluidine method; DPG concentration was determined by a nonenzymatic method [2]. Blood for the tests was taken by puncturing the lateral auricular vein of adult rabbits, puncture of the femoral vein of neonates and jugular vein of 7-day-old animals, and by means of decapitation of golden hamsters.

Results and Discussion

Table 1 lists the results of assaying AHO in hypoxic (5000 m) animals. Preliminary experiments revealed that there was an increase in AHO in cats given hexenal or ether anesthesia before taking blood samples. The value of p50 (partial oxygen tension at which there is 50% oxygenation of hemoglobin) dropped from 38.6±0.2 mm Hg in the control to 35.8±0.5 mm Hg ($n = 11$, $P<0.001$). In view of the fact that anesthesia leads to shifting of the curves of oxyhemoglobin dissociation and distorts the true values of p50, in subsequent experiments we did not use anesthetics.

As shown by control readings, the oxygen-binding property of hemoglobin was significantly lower in adult animals than neonates. AHO was lower in cats than rabbits. The species- and age-related differences in values of p50 were highly reliable ($P<0.001$ and $P<0.01$); the dissociation curves were shifted to the left by 11 mm in neonate rabibts and by a mean of 4 mm Hg in newborn kittens. AHO was also higher in 7-day kittens than in adult cats ($P<0.001$). Hemoglobin did not differ in oxygen-binding property in some newborn and 7-day kittens from the value in adult cats.

Table 1.
DPG in hypoxic animals (p50, mm Hg)

Age of animals	Control	Hypoxia 500 m
Cats		
Adult	38,6±0,2 (15)	32,6±0,4 (15)**
7 days	35,7±0,5 (16)	33,6±0,4 (16)*
Neonate	34,2±1,5 (5)	38,6±0,8 (5)*
Rabbits		
Adult	30,4±0,3 (17)	33,0±0,4 (16)**
Neonate	19,1±0,5 (11)	24,2±0,6 (8)**

Note: Here and in Table 2, the number of animals is given in parentheses
*P<0.01 **P<0.001

Table 2.
Blood parameters of hypoxic golden hamsters

Conditions	DPG, μM/mℓ	Glucose, mg%
Control	4,56±0,17 (20)	33,75±2.0 (6)
Hypoxia:		
5000 m	7,34±0,20 (26)	61,56±7,7 (8)
7000 m	5,33±0,65 (7)	43,68±3.6 (11)

There were opposite hemoglobin reactions in response to hypoxic hypoxia in cats and rabbits. In adult and 7-day cats AHO increased and in rabbits it decreased. A significant decline of AHO was inherent in neonate animals of both species. In neonate kittens, the dissociation curves, which shifted to the right, reached the positions of dissociation curves for adult cats. On the basis of the conception that a shift to the right of dissociation curves leads to better delivery of oxygen to body tissues, the fact that there was a right shift of dissociation curves in rabbits and newborn kittens could be interpreted as a compensatory reaction. In this case, one should seek the cause of decreased AHO in a change in intraerythrocyte environment, since the time of exposure of animals to hypoxia was insignificant to appearance of hemoglobin with altered structure in blood. It is known that the DPG content increases in hypoxic animals, including rabbits, as a result of activation of glycolysis in erythrocytes, which results in a right shift of dissociation curves [3]. However, elevation of DPG level in erythrocytes is apparently limited to a specific range, depending on level of partial oxygen tension. Thus, the concentration of DPG increased by 35% (P<0.001) and glucose by 82% in golden hamsters (Table 2) raised to an "altitude" of 5000 m; at an "altitude of 7000 m, no changes were demonstrable in DPG concentration, although glucose concentration in blood was almost 30% above normal (P<0.05). It should be expected that there would be a decrease of AHO following the change in erythrocyte DPG level in golden hamsters when raised to an "altitude" of 5000 m.

In view of the fact that energy resources of newborn kittens and rabbits are maintained primarily via the glycolytic anaerobic pathway, a right shift of their dissociation curves in the presence of hypoxia could also be attributed to activation of glycolysis and accumulation of DPG in blood. There was minimal glycolytic activity in the direction of the DPG shunt in erythrocytes of adult cats; the concentration of this phosphate constitutes a mean of 1 μM/mℓ cells [4]. For this reason, it is difficult to attribute the change in AHO of hypoxic cats to the dynamics of blood phosphates. In this case, the mechanism of regulation of oxygen-binding property of hemoglobin due, in our opinion, to a shift of erythrocyte pH in the alkaline direction as a

result of increase in share of deoxygenated hemoglobin and increased transport of carbon dioxide from the organism. Ultimately, the shift of dissociation curves of rabbits and cats is determined by pH dynamics, but in rabbits this process is mediated by accumulation of DPG, whereas in cats the change in pH has a direct effect on the hemoglobin molecule.

The meaning of the shift of oxyhemoglobin dissociation curves to the left in adult cats remains unclear. In this case, there is decreased transport of oxygen by the cells of an organism that is already experiencing a shortage of oxygen. It has now been proven that the oxygen-binding property of hemoglobin of many animal species is enhanced under hyperoxic conditions, and that this is one of the protective mechanisms to prevent excessive access of oxygen to tissues. However, AHO decreases in hyperoxic cats [5]. We can see on the example of the hemoglobin reaction of cats that it does not simply transport oxygen, but its normal function is possible only with a specific blood pO_2 level, since AHO increases when there is an O_2 deficiency and decreases with excessive amounts thereof.

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CHANGES IN RABBIT IMMUNOREACTIVITY AS RELATED TO DURATION OF HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA In Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 18 Dec 80) pp 90-91

[Article by V. V. Tyavokin, V. N. Sizov, G. V. Magnitskaya and Ye. A. Oleynikova]

[Text] In this century of scientific and technological revolution, the consequences of progressively decreasing muscular activity of people due to mechanization of industry and housekeeping aids ["improvements"] are becoming one of the pressing medical problems.

We encountered only a few and incomplete reports in the available literature concerning the effect of hypokinesia on the body's immune system [1-4].

We conducted this study in order to examine the effects of hypokinesia differing in duration and readaptation period on the body's *nonspecific defense factors.*

Methods

Experiments were conducted on 30 male chinchilla rabbits. Their weight ranged from 2.5 to 3 kg (2.7 kg average). The animals were placed in a special cage to restrict movements [5]. We made a distinction between three degrees of hypokinesia: moderate, when the animals were kept in the usual cages; average, created by placing the animals in a special cage, where the space between the sides of the cage and animal constituted more than 2 cm (the rabbit was able to move along the length of the cage); severe, when the space between the rabbit and sides of the special cage constituted 1-2 cm.

We conducted our studies in the presence of average hypokinesia. No change in restriction of animal movements was made when they were fed or blood samples taken.

We selected the following as tests to determine the intensity of spontaneous immunity: bactericidal, lysozyme, beta-lysine, blood serum complement activity and *neutrophil phagocytic reaction*, which consisted of phagocytotic activity (PA), intensity (IP) and completion of phagocytosis (CP).

We made a dynamic study of spontaneous resistance factors: before restricting movement, after 5, 10, 15, 30 days of hypokinesia and in the readaptation period--7 days after 15- and 30-day hypokinesia.

Results and Discussion.

Table 1 lists the results of our studies. The changes in nonspecific immune mechanisms were phasic, and they depended on duration of hypokinesia. Thus, at the early stage (5 days), the most labile humoral nonspecific defense mechanisms were bactericidal ($P<0.05$) and beta-lysine ($P<0.001$) activity of blood serum. At the same time, we must note that they changed in different directions: increase of the former and decrease of the latter. IP and CP of neutrophils were depressed after 5 days of hypokinesia.

Table 1. Spontaneous resistance factors under hypokinetic conditions (M±m)

Activity	Before hypokinesia	Hypokinesia, days			
		5	10	15	30
Bactericidal	98,89±6,72	130,2±13,04*	107,5±5,65**	109,13±2,91**	100,0±4,69**
Lysozyme	5,40±0,27	5,10±0,72**	2,07±0,45***	1,60±0,31***	2,71±0,46*
Complement	4,37±0,09	4,45±0,08**	4,42±0,09**	4,53±0,25**	5,06±0,66**
Beta-lysine	0,32±0,03	0,19±0,003***	0,11±0,02***	0,11±0,02***	0,10±0,02*
PA	72,96±1,01	74,44±2,49**	82,13±1,07***	83,07±0,98***	87,75±1,85***
IP	4,65±0,24	2,48±0,18***	3,37±0,06***	3,26±0,08***	7,93±0,76***
CP	0,93±0,02	0,72±0,05***	0,87±0,03**	0,49±0,06*	0,55±0,06***

Here and in Table 2: *P<0.05 **P>0.05 ***P<0.001

Table 2. Spontaneous resistance factors in readaptation period

Activity	Before hypokinesia	7 days after 15-day hypokinesia	7 days after 30-day hypokinesia
Bactericidal	98,89±6,72	105,78±4,34**	87,50±2,61*
Lysozyme	5,40±0,27	2,53±0,29***	0,98±0,14***
Complement	4,37±0,09	1,92±0,18***	4,78±0,32**
Beta-lysine	0,32±0,03	0,21±0,006**	0,17±0,07**
PA	72,96±1,01	62,22±1,17***	85,86±1,06***
IP	4,65±0,24	5,96±0,09***	5,28±0,84**
CP	0,93±0,02	0,80±0,06*	0,59±0,06***

As duration of hypokinesia increased (10 and 15 days), there was increased deregulation of nonspecific defense mechanisms. We observed further decline of beta-lysine level to 0.11±0.02 with concurrent decrease in blood serum lysozyme concentration to 1.60±0.31 mg/mℓ ($P<0.001$). The direction of changes in IP and CP of neutrophils was the same as at the early stage of hypokinesia, and the differences were quantitative. There was concurrent further and reliable increase in amount of active phagocytes (to 83.07±0.98%), which was apparently compensatory in nature. By the 30th day of hypokinesia these changes essentially persisted.

The nature of immunological changes in the readaptation period was related to duration of prior hypokinesia (Table 2). Thus, 1 week after 15-day restriction of movement of the animals, only 2 out of the 7 tested parameters reached the base level--bactericidal and beta-lysine activity of blood serum, i.e., the ones

that were the first to change during hypokinesia. The drastic decrease in concentration of complement merits special attention, since the value of this parameter did not differ from initial figures ($P>0.05$) in the case of 15-day restriction of movement. Evidently, this was related to insufficient complement synthesis or utilization thereof by the immune complex. At the same stage, we observed a tendency toward normalization of the phagocytic reaction. There was a decrease in number of active phagocytes with concurrent intensification of their absorptive and digestive capacity, which was indicative of an increase in protective potential of the phagocytic process.

We were impressed by the state of nonspecific defense factors in the readaptation period following 30-day hypokinesia. There was a decrease in deregulation of nonspecific defense mechanisms after 30-day hypokinesia and restoration of spontaneous resistance factors after 15-day hypokinesia. Thus, while bactericidal activity of serum was at the base level 7 days after 15-day hypokinesia, it was reliably diminished 7 days after 30 days of hypokinesia. Blood serum lysozyme activity presented a tendency toward increase 7 days after 15-day hypokinesia, whereas a drastic decrease was demonstrated 7 days after 30-day hypokinesia.

It is imperative to conduct further studies to examine the effects of hypokinesia differing in degree and duration, as well as of the readaptation period, on parameters of nonspecific defense of the organism.

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DISCUSSIONS

UDC: 613.693:612.821.1/.3

COMPARATIVE ANALYSIS OF PERSONALITY TRAITS OF FIRST TO FOURTH YEAR PILOT CADETS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 (manuscript received 15 Mar 79) pp 91-94

[Article by Ye. V. Bannov and V. S. Lozinskiy]

[Text] Flight training imposes high demands of the cadet's personality. Instruction at flying VUZ's includes acquisition of knowledge, skills and abilities with reference to piloting modern aircraft.

Flight work, which is characterized by high speed and intensity of the work process in the presence of increased emotional tension [stress] and responsibility for the quality and outcome of each flight assignment, leaves its imprint on the personality of a pilot cadet.

Data are cited in the literature concerning studies of personality traits of cadets, pilots, navigators, operators, students and athletes with the use of projective tests [1-9]. In particular, F. B. Berezin et al. studied the personality distinctions of first to third year medical institute students. They traced the development of professionally significant personality traits in medical students during the period of VUZ training.

Comparative analysis of personality traits of first-year cadets and flying school graduates is of particular interest, since it discloses the dynamics of development of different professionally important personality traits in a pilot, and it is important to take this into consideration in the course of psychological screening for flying VUZ's and psychophysiological training of cadets for flights.

It is possible to perform this task by making a dynamic study of the comparative traits of first- to fourth-year flying school cadets.

Methods

We studied first- to fourth-year flight VUZ cadets. Psychological features were studied by means of the standardized method of personality study (SMPS) and 16-factor personality questionnaire (PQ). Along with personality tests, we held individual talks, the purpose of which was to examine the cadets' personality traits and define the results of tests made by the personality methods. We also used data obtained from observing the cadets during the training process, as well as the results of examinations performed in the course of psychological screening. In all, we studied 1044 cadets. The questionnaires were used and

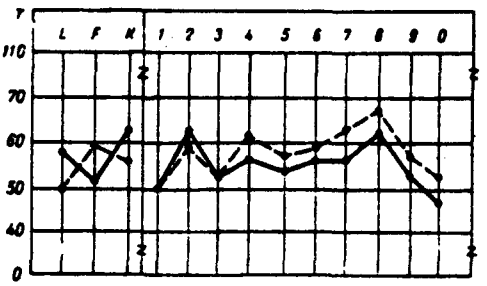

Figure 1.
Averaged data on first-year (solid line) and fourth-year (dash line) cadets by the SMPS method

L, F, K) scales for determining reliability of test performance
1) extent of subject's fixation on his health
2) tendency toward excitement, control of emotions
3) emotional lability, social pliability, conformism
4) tendency to take chances, impulsiveness, marked exactingness
5) male and female character traits, orientation of sexual preference
6) rigidity of judgements, "hardness" of sets, insistence, stubbornness
7) anxiety, psychasthenic traits
8) originality of thinking and perception, intuitiveness
9) level of activity and optimism
0) social introversion--extraversion

examination performed at the time of admission to the school and after completion by the cadets of the first, second, third and fourth years of study. In all, we conducted 2662 tests with the use of the SMPS, 2918 with the use of questionnaires with the PQ (forms B and A+B in "raw" factors and "sten") and 1118 talks. The obtained data were submitted to statistical processing on computer.

We considered the following parameters for interpretation of the obtained data: arithmetic mean (AM) of 33 tested personality traits; standard deviation (SD) of parameters; mean error of mean value; the coefficient corresponding to SD/AM; reliability of differences between compared parameters.

Results and Discussion

The averaged profiles of first and fourth year cadets, tested by the SMPS and PQ are illustrated in Figures 1 and 2. The parameters of personality traits of the subjects were in the range of the norm established by the authors of the original and adpated variants [8, 10, 11].

The SMPS profile of cadets screened for flight VUZ training and school cadets did not exceed a score of 70/T on any of the scales.

For enrollment at flight VUZ's, the candidates had to undergo a psychological examination and comprehensive medical certification in order to screen individuals in the best of health with a high score for professionally important mental functions.

Analysis of the obtained averaged SMPS profiles enabled us to demonstrate some basic personality traits in common for the cadets in the lower and higher years of training.

The personality traits of both first-year cadets and graduates were characterized by such parameters as activity, energy, sociability, self-confidence, decisiveness, courage, goal orientation, well-developed sense of duty, responsibility, vivid emotionality and high degree of self-control.

At the same time, there were some personality distinctions inherent in the different groups we compared. Thus, fourth-year cadets were characterized by self-

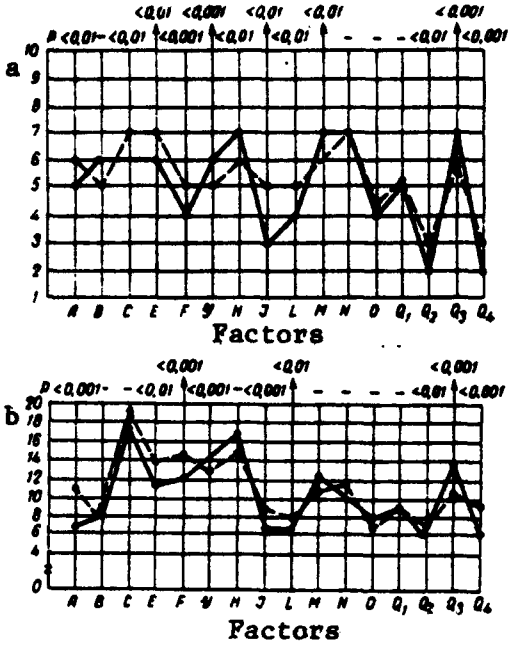

Figure 2.
Averaged PQ data in stens (a) and in "raw scores" (b) for first-year (solid line) and fourth-year (dash line) cadets

A) restraint--gregariousness
B) concrete thinking--abstract thinking
C) sensitivity--resistance, rationality
E) compliability--domination
F) seriousness--joyfulness
G) initiative--painstaking
H) lack of confidence--decisiveness
I) emotional maturity, realistic--tendency toward fantasizing, refinement
L) trust, adaptability--inflexibility, preference for one's own opinion
M) practicality--impracticality
N) guilelessness--calculating
O) self-confidence--anxiety
Q_1) conservatism--innovativeness
Q_2) dependence on group--independence
Q_3) internal conflict--self-control
Q_4) relaxed calm--high motivation

confidence, high level of exactingness, desire for leadership, high self-appraisal, activity, gregariousness and willingness [desire] to take chances. They were emotional, and characterized by some degree of impulsiveness with good self-control. They had a well-developed sense of duty, responsibility, firmness of convictions and sets.

The averaged profile of first-year cadets differed from the profile of higher-year ones with regard to such traits as desire to show oneself in the best possible light, unstable mood, impulsiveness with some decline of control of emotions and high self-appraisal.

A comparison of average SMPS profiles according to Student's t criterion of first and fourth year cadets revealed lower parameters on scale l ($P<0.001$), somewhat higher ones on scale F ($P<0.05$) and reliably lower ones ($P<0.001$) on scale K for the senior group of cadets.

The senior cadets were characterized by a more stable mood (scale D, $P<0.01$; scale Pa, $P<0.01$) and stronger emotional control, as compared to first-year cadets (higher parameters on scale 5, $P<0.001$, scale Pt, $P<0.001$) and high activity (scale Ma, $P<0.001$).

Analysis of the SMPS results revealed that most of the subjects could be classified among four main types.

The first of these types was referable to 5.3% of all cadets (11% in the first year and 3% in the fourth), who presented high scores on scales 2, 7, 0 (in different combinations). These were individuals with a tendency toward anxiety reactions, marked desire to avoid failure by greater control of their actions, meticulous preparation for classes, tests, flights and thinking out (playing through, verbalizing) elements of activity. They were notable for applying themselves, being tense in a novel and unusual situation, passive in public life and susceptible to suggestion. They were characterized by a low self-appraisal, insufficient initiative and a limited circle of socialization. More than one-third of such cadets were dismissed from the school: 18% due to poor achievement in flight studies, 11% for medical reasons and 4% at their own desire.

Individuals with significantly higher scores on scales 4, 6, 8 and 9 (in different combinations) and somewhat higher scores on scale 2 can be classified as the second type. This type was referable to 2.7% of all cadets (7% first and 2% fourth year). These individuals were characterized by a high level of motivation and activity, marked tendency toward competition, great optimism, courage, daring, tendency to take chances, combined with emotional immaturity, impulsiveness, stubbornness and excessive confidence in one's own stand. It is difficult for them to make contact, they overestimate their own capabilities, disregard the authority of teaching personnel, which creates considerable difficulties for the pilot instructor. More than half of the cadets with these personality traits were dismissed from school: 36% for lack of discipline, 8% for poor achievement and 8% at their own desire.

The third type of cadets are characterized by moderately elevated scores on scales 4, 6, 8, 9 and 2, 5, 7 and 0 (in different combinations).

Such cadets constituted the absolute majority (80% in the first year and 93% in the fourth). These are balanced individuals, who are entirely satisfied with their position and capabilities. They are characterized by self-confidence, marked exactingness and self-appraisal, activity and gregariousness. They are emotional, adequately aggressive and decisive. They have a well-developed sense of duty and responsibility. Cadets of this type were dismissed from school on the following grounds: 7% for poor achievement, 5% for medical reasons and 2% for lack of discipline.

The smallest group (2%) consisted of individuals whose leading scores were on scales 1 and 3, combined with high scores for different variants of scales 6, 8 and 9. They constituted 4% of the first-year cadets and 2% of the fourth-year ones. According to the classification of Leonhard [12], such cadets are individuals with marked signs of rigidity, demonstrativeness and hyperthymia. Of such cadets, 30% were dismissed: 22% for medical reasons, 4% at their own wish and 4% for poor achievement in flight training.

It should be noted that the averaged profiles of the lower-grade cadets were identical in many respects to those demonstrated in the studies of N. F. Luk'yanova, whereas those of the senior cadets were similar to the profiles in a group of pilots [5, 6]. According to the PQ, the profiles of first- and fourth-year cadets also presented statistically significant differences. They were demonstrable when we compared the averaged profiles expressed in both stens and "raw scores" (factors) (see Figure 2).

The senior cadets differed reliably from first-year ones with regard to factors A ($P<0.001$), E ($P<0.01$), F ($P<0.001$), G ($P<0.001$), I ($P<0.001$), L ($P<0.001$), Q_2 ($P<0.01$), Q_3 ($P<0.001$), Q_4 ($P<0.001$) and F_1 ($P<0.001$). In addition, the differences in compared results were reliable in stens for factors C and M ($P<0.01$).

These parameters characterize the senior cadets, as compared to first-year ones, as being more energetic, with greater initiative, resourcefulness, self-confident, firm in their decisions, brave, practical, independent with adequate self-control and high motivation.

The junior cadets were notable for trying harder, being conscientious, sensitive, trusting, adaptable in a group, some degree of dependence, high self-appraisal and lower level of motivation than in fourth-year cadets.

In addition, the first-year cadets presented higher scores, of 7 sten or more, for factors G (27%), H (54%), M (61%), Q_1 (20%) and Q_3 (58%); down to 4 sten or less for factors F (68%), I (41%), L (24%), Q_2 (82%), Q_3 (7%), Q_4 (23%) and F_1 (71%). In fourth-year cadets, scores were elevated to 7 or more sten for factors A (21%), C (48%), F (9%), I (6%), L (24%), Q_4 (63%), F_2 (57%), and scores of 4 sten or less for factors G (9%), H (9%), M (6%), N (9%), Q_1 (21%), F_2 (9%), F_3 (15%) and F_4 (30%). Among first-year cadets, average values (4-6 sten) for factor F were encountered in 32% and among fourth-year cadets in 79%; this applied to factor Q_2 in 15 and 28%, respectively, Q_4 in 77 and 37%, F_2 in 70 and 34%, F_4 in 83 and 55%.

The obtained data indicate that senior cadets have more marked personality traits such as courage, decisiveness, energy, composure, independence, persistence in reaching goals, high degree of self-control and practicality. In first-year cadets these traits were less pronounced.

Thus, studies of personality traits of flight cadets using the SMPS and PQ methods make it possible to demonstrate changes in various professionally important features in pilot cadets during the period of training at a school. The obtained data should be taken into consideration when conducting psychological screening of applicants for flight VUZ's, as well as in psychophysiological training of cadets for different types of flights.

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NEW BOOK ON HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 15, No 4, Jul-Aug 81 pp 94-95

[Review by P. V. Vasil'yev of book "Gipokinezia" (Hypokinesia) by Ye. A. Kovalenko and N. N. Gurovskiy, Moscow, Meditsina, 1980, 319 pages]

[Text] This monograph deals with one of the pressing problems of modern medicine--effect on man of drastic decrease in muscular activity due to the intensive development of technology, mechanization and automation of industry in this age of scientific and technological revolution. It is also extremely important to study hypokinesia and hypodynamia for broad clinical practice, particularly if patient treatment involves compulsory and long-term restriction of movement, bed rest or immobilization of different parts of the body. The authors observe that restriction of motor activity and force loads is of special interest to space, marine, submarine and polar medicine. In recent years, there has been intensive work on this problem in scientific institutions of both our country and abroad. However, in spite of a number of publications, a generalization of the basic aspects of this problem had not been offered in the literature up to this time.

This monograph is the first major generalization of both the facts gathered by the authors and numerous publication sources referable to Soviet and foreign researchers. This book was written by well-known authors, on the basis of a general biological approach to the problem, drawing upon clinical, physiological, biochemical and morphological data. It begins with a comprehensive foreword by Academician O. G. Gazenko, in which the timeliness of the book is validated and a brief description is given.

The Introduction comments on the significance of hypodynamia and hypokinesia as one of the leading problems of the late 20th century. Special attention is given to the significance of the issues discussed to a wide range of specialists in space, marine and sports medicine.

Chapter 1 describes in detail the methods of model reproduction of different variants of hypokinesia in both animals and man. The methods of conducting such studies in clinical practice are described.

In Chapter 2, data are given on the changes in gas and energy metabolism under hypokinetic conditions. In presenting the material, a link is constantly made between the observed changes on the level of the whole organism and deviations that occur at first on the molecular and submolecular levels, as well as tissues and organs.

Chapter 3 deals with the changes and disturbances that occur under hypokinetic conditions with reference to morphology and biochemistry of the heart. Comprehensive data are submitted on changes in the vascular system, in particular, disturbances referable to microcirculation and tissular oxygenation. Special attention is given to the "premorbid" state elicited by hypokinesia and the danger of subsequent development of cardiovascular pathology. The effect of hypokinesia on both essentially healthy subjects and those suffering from cardiovascular disease is described. It is indicated that hypokinesia plays some part in disturbances of lipid metabolism and development of atherosclerosis.

The fourth chapter analyzes data on the effect of hypokinesia on the muscular system. The changes in work capacity, strength and endurance of muscles are described in detail. There is discussion of the severity and depth of disturbances referable to coordination of movements, muscle tone, excitability, contractility and bioelectrical activity of muscles. The morphological and biochemical changes, which occur in muscles, are described and details given on electron microscopic and histochemical findings in the muscular system. The general characteristics of the effects of diminished muscular activity on body functions and processes of neuroendocrine regulation thereof are described in the conclusion [to this chapter].

Chapter 5 describes the changes in the bone system in the case of restricted movement. Analysis is made of the effect of hypokinesia on mass and growth of bones, change in density, structure and histology of osseous tissue. Distinctions are noted in metabolism of bone tissue, as well as calcium, phosphorus and protein metabolism. The effect of hypokinesia on general metabolic changes in decalcified tissues is stressed. There is discussion of changes in the bone system and their effects on function of other organs and body as a whole.

Chapter 6 offers an analysis of general pathogenesis of long-term hypokinesia and hypodynamia from the standpoint of pathological physiology. There is discussion of the prime etiological factor, demonstration of the main elements of pathogenesis, occurrence of vicious circles and ultimate disturbances in a number of body systems. For the first time, the question is raised of possible quantitative and qualitative changes caused by hypokinesia as the distinctive onset of pathological disturbances and possible development of "hypokinetic disease." An original general scheme of the pathogenesis of hypokinesia is offered. True, the authors' desire to cover all elements of pathogenesis resulted in an extremely complex scheme, which makes it difficult to comprehend.

There are theses in this work that could serve as a fruitful basis for discussion and, consequently, for conducting more studies of this important problem. In the conclusion, there is brief indication of the possible routes for preventive measures, as well as rehabilitation after hypokinesia.

This book is well-illustrated with figures, microphotographs, graphs and diagrams. The main bibliography dealing with hypokinesia is furnished at the end.

This monograph is intended for a wide circle of clinicians (primarily surgeons and general practitioners), physiologists, pathophysiologists, physicians in space, marine and sports medicine, as well as specialists at scientific and medical institutions concerned with the problem of hypodynamia and hypokinesia in both the scientific and purely applied aspects, for the purpose of working out rehabilitation and preventive measures to eliminate their adverse effects on the organism.

ABSTRACTS OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE OF MEDICAL AND MEDICOTECHNICAL INFORMATION

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EFFECT OF LONG-TERM LACK OF MOTOR ACTIVITY ON FUNCTIONAL STATE OF SPINAL CORD MOTONEURONS

[Abstract of article by S. A. Skuratova, V. S. Oganov and M. A. Shirvinskaya]

[Text] On the basis of a study of monosynaptic and polysynaptic reflexes, the effects of long-term (75 days) restriction of movement on the functional state of flexor and extensor motoneurons of the rat spinal cord were investigated. The threshold of excitability, latency period and amplitude-time characteristics of monosynaptic and polysynaptic reflexes, recorded in the form of bioelectrical responses of the anterior radices of the spinal cord to stimulation of peripheral nerves, served as the main criteria for evaluation of the state of motoneurons. Studies were also made of the nature and magnitude of effects of posttetanic potentiation (PTP) and presynaptic inhibition (PSI). It was established that long-term restriction of movement is associated with appareciable functional changes in the segmental system of the spinal cord, which differed in direction in extensor and flexor pools of motoneurons. The aggregate of data is indicative of diminished excitability or depression of activity of extensor motoneurons as a result of the experimental factor, as manifested by elevation of threshold of excitability, decline of amplitude and duration of monosynaptic responses. Concurrently, there was alleviation of PTP effects and more marked PSI of extensor motoneurons. The changes described with monosynaptic and polysynaptic testing of flexor motoneurons may be indicative of development of lasting excitation in them, as manifested by an increase in amplitude and shortening of latency period of monosynaptic responses. This hypothesis is not in contradiction with data concerning reduction of overall area of polysynaptic discharges and depression of the PTP effect. The nature of change in reflex activity of flexor motoneurons coincides in many respects with the electrophysiological manifestations of "excitation deficiency." There is reason to assume that the changes demonstrated in this study with reference to reflex activity of spinal cord motoneurons are related to change in nature of afferent impulsation from proprioceptors of the corresponding muscles, as a result of different biomechanics of contraction thereof under hypokinetic conditions. The change in nature of reflex activity of motoneurons could lead to change in pattern of controlling influences of the nervous system on muscles, and these changes may vary

in functionally different specialized units. This is consistent with the demonstrated differences between changes in physiological properties of fast and slow skeletal muscles of rats after analogous treatment (restricted movement) and the 22-day space flight with rats aboard biosatellites of the Cosmos series. Thus, analysis of the results of this study shows that there is experimental confirmation of the existing view of possible role of change in neuromuscular trophic correlations in mechanisms of adaptation of skeletal msucles to relative inactivity and, in particular, weightlessness.

Illustrations 2; bibliography lists 24 items.

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COMPARATIVE EVALUATION OF HYPERBARIC NORMOXIC NITROGEN- AND HELIUM-OXYGEN MIXTURES IN SOME BIOCHEMICAL STUDIES

[Abstract of article by Ye. A. Zagorskaya and I. I. Lyubarskaya]

[Text] Brief bibliographic references are cited concerning the question of effects of high helium pressure on the organism in the area of biochemical studies. Data are submitted on levels of hormonal compounds: 11-hydroxycoricosteroids in blood, 17-ketogenic and 17-ketosteroids in 24-h urine, lipid fractions--total lipids,triglycerides, free fatty acids, β-lipoproteins, phospholipids, total cholesterol--in blood of 6 professional divers during and after dry "immersion," in a hyperbaric chamber in an atmosphere of nitrogen-oxygen and helium-oxygen mixtures to a pressure of up to 32 and 55 mm water column using different rates of compression. Analysis is made of the obtained results.

Bibliography lists 21 items.

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